Making Healthcare Safer IV

Opioid Stewardship

Rapid Review

Structured Abstract

Objectives. Opioid stewardship interventions promote the appropriate use of prescribed and ordered opioids to reduce the risk of opioid adverse events. Our main objectives were to determine the effectiveness of these interventions in healthcare settings on opioid prescribing and clinical outcomes (e.g., number of opioid prescriptions, opioid dosage, overdose, emergency department visits, and hospitalizations) including unintended consequences (e.g., changes in patient-reported pain intensity), and ways these interventions can be effectively implemented.

Methods. We followed rapid review processes of the Agency for Healthcare Research and Quality Evidence-based Practice Center Program. We searched PubMed and the Cochrane Library to identify eligible systematic reviews from January 2019 to April 2023 and primary studies published from January 2016 to April 2023, supplemented by targeted gray literature searches. We included systematic reviews and studies that addressed opioid stewardship interventions implemented in healthcare settings in the United States and that reported on opioid prescribing and clinical outcomes.

Findings. Our search retrieved 6,431 citations, of which 34 articles were eligible (including 1 overview of systematic reviews, 13 additional systematic reviews, 13 randomized controlled trials (RCTs) [reported in 14 articles] and 6 nonrandomized studies). Systematic reviews, mostly summarizing pre-post studies, included a wide variety of opioid stewardship practices that focused on patient and family engagement, healthcare organization policy, or clinician knowledge and behavior interventions, in inpatient, perioperative, emergency department, and ambulatory settings. RCTs addressed multicomponent interventions (typically a combination of prescriber education, care management and facilitated access to resources), and patient education and engagement, mainly in ambulatory chronic pain. Opioid stewardship practices involving clinical decision support or electronic health records, or multicomponent interventions (including for chronic pain) were associated with decreases in opioid prescribing or reduced doses and no increases in pain, emergency department visits, or hospitalizations (low strength of evidence for all outcomes). Patient engagement and

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education interventions had mixed results for opioid prescribing outcomes (insufficient strength of evidence) and no increases in pain, emergency department visits, or hospitalizations (low strength of evidence). The evidence was insufficient on other types of interventions and on outcomes of opioid refill requests and refills, patient satisfaction, or overdose. Barriers included lack of training, workload, gaps in communication, and inadequate access to nonpharmacological resources. Facilitators included clinician and patient acceptance of intervention components.

Conclusions. Selected opioid stewardship interventions may be effective for reducing opioid prescribing and dosing without adversely affecting clinical outcomes overall, although strength of evidence was low. Unintended consequences were often not measured or not measured rigorously. Interventions to reduce opioid use should monitor unintended consequences and include access to nonpharmacological pain management resources with appropriate patient education and engagement.

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1. Background and Purpose

The Agency for Healthcare Research and Quality (AHRQ) Making Healthcare Safer (MHS) reports consolidate information for healthcare providers, health system administrators, researchers, and government agencies about practices that can improve patient safety across the healthcare system—from hospitals to primary care practices, long-term care facilities, and other healthcare settings. In spring 2023, AHRQ launched the fourth iteration of the MHS report (here referred to as MHS IV). Opioid stewardship was identified as high priority for inclusion in the MHS IV reports using a modified Delphi technique by a Technical Expert Panel (TEP) that met in December 2022. The TEP included 15 experts in patient safety with representatives of governmental agencies, healthcare stakeholders, clinical specialists, experts in patient safety issues, and a patient/consumer perspective. See the MHS IV Prioritization Report for additional details.[1]

The treatment of pain and suffering is fundamental to high-quality healthcare, and opioids are often an essential medicine for acute, severe pain. However, opioids also carry well known risks, including overdose, misuse and opioid use disorder.[2-4] In 2016, the Centers for Disease Control and Prevention (CDC) released a Clinical Practice Guideline for Prescribing Opioids for Pain to promote more effective and safe opioid prescribing. In 2022, the CDC released an update to those guidelines, noting a concern that previous guidance had been misapplied, leading to unintended patient harm including untreated or undertreated pain and abrupt discontinuation of opioids causing withdrawal, distress, and suicidal ideation. Thus, any patient safety practice (PSP) to mitigate risks of prescribed or ordered opioids should be balanced against unintended harms.[3]

1.1 Overview of the Patient Safety Practice

Opioid stewardship can be defined as promoting the appropriate use of prescribed and ordered opioids while reducing the risk of opioid use disorder, misuse, overdose, and other adverse events.[3] The National Quality Forum (NQF) identified fundamental actions to support opioid stewardship in healthcare organizations,[5] six of which are relevant to this report:

- Promote leadership commitment and culture,
- Implement organizational policies,
- Advance clinical knowledge, expertise, and practice,
- Enhance patient and family caregiver education and engagement,
- Track, monitor, and report performance data, and
- Establish accountability.

The updated 2022 CDC Clinical Practice Guideline for Prescribing Opioids for Pain provides guidelines for determining whether opioids are appropriate, deciding duration, dosage and followup for prescriptions, and assessing risk and addressing potential harm.[3]

The MHS III report conducted a targeted search of the literature and summarized one systematic review and 14 original studies on this topic, mainly pre-post studies.[6] In that limited review, most studies examined multicomponent interventions consisting of clinical interventions and implementation strategies, with a conclusion of moderate strength of evidence for only one outcome—significant reduction in opioid dosages. MHS III did not draw conclusions about clinical outcomes or impact on pain.

1.2 Purpose of the Rapid Review

The overall purpose of this review is to determine the effectiveness of opioid stewardship interventions in healthcare facilities or systems on key opioid prescribing and clinical outcomes (e.g., opioid dosage, opioid prescriptions, overdose, emergency department visits, and hospitalizations) including unintended consequences (e.g., changes in pain intensity), and how these interventions can be effectively implemented.

1.3 Review Questions

1. What are the frequency and severity of harms associated with opioid prescribing and ordering (i.e., outpatient prescribing or inpatient ordering)?
2. What patient safety measures or indicators have been used to examine the harms associated with opioids prescribed or ordered by clinicians?
3. What opioid stewardship PSPs have been used to prevent or mitigate the harms associated with prescribed or ordered opioid, and in what settings have they been used?
4. What is the rationale for the opioid stewardship practices that have been used to prevent or mitigate the harms associated with prescribed or ordered opioids?
5. What are the effectiveness and unintended effects of opioid stewardship practices, and what new evidence has been published since the search was done for the MHS III report in 2019?
6. What are common barriers and facilitators to implementing opioid stewardship practices?
7. What resources (e.g., cost, staff, time) are required for implementation of opioid stewardship practices?
8. What toolkits are available to support implementation of opioid stewardship practices?

2. Methods

We followed processes proposed by the Agency for Healthcare Research and Quality (AHRQ) Evidence-based Practice Center (EPC) Program.[7] The final protocol for this rapid review is posted on the AHRQ website at: https://www.ahrq.gov/research/findings/making-healthcare-safer/mhs4/index.html. The protocol for this rapid review is registered in PROSPERO (registration number CRD42023432272).

For this rapid review, strategic adjustments were made to streamline traditional systematic review processes and deliver an evidence product in the allotted time. Adjustments included being as specific as possible about the questions, limiting the number of databases searched, modifying search strategies to focus on finding the most valuable studies (i.e., being flexible on sensitivity to increase the specificity of the search), and restricting the search to studies published in English and performed in the United States (to be most relevant to healthcare systems in the United States). For this report, we used the artificial intelligence (AI) feature of DistillerSR (AI Classifier Manager) as a second reviewer at the title and abstract screening stage.

We asked our content experts to answer Review Questions 1 and 2 by citing selected references that best answer the questions without conducting a systematic search for all evidence on the targeted harms and related patient safety measures or indicators. For Review Question 2, we focused on identifying relevant measures that are included in the Centers for Medicare & Medicaid Services (CMS) patient safety measures, AHRQ's Patient Safety Indicators, or the National Committee for Quality Assurance (NCQA) patient safety related measures. We asked content experts to answer Review Questions 3 and 4 by citing selected references, including patient safety practices (PSPs) used and explanations of the rationale presented in the studies we found for Review Question 5. For Review Questions 6 and 7, we focused on the barriers, facilitators, and required resources reported in the studies we found for Review Question 5. For Review Question 8, we identified publicly available patient safety toolkits developed by AHRQ or other organizations that could help to support implementation of the PSPs. To accomplish that task, we reviewed AHRQ's Patient Safety Network (PSNet) and AHRQ's listing of patient safety related toolkits and we included any toolkits mentioned in the studies we found for Review Question 5.[8,9] We identified toolkits without assessing or endorsing them.

2.1 Eligibility Criteria for Studies of Effectiveness

We searched for original studies and systematic reviews on Review Question 5 (the question addressing effectiveness studies) according to the inclusion and exclusion criteria presented in Table 1.

Table 1. Inclusion and exclusion criteria

Study Parameter	Inclusion Criteria	Exclusion Criteria
Population	Any clinical population (i.e., people receiving care from a healthcare professional) Because opioids can result in significant harms in any clinical population, we will include populations not included in the CDC guidelines, such as sickle cell disease, cancer-related pain treatment, palliative care, and end-of-life care	None

Intervention	• Interventions focused on opioid stewardship involving organizational leadership and policies within a healthcare facility or healthcare system:
	  ○ Opioid stewardship committees
	  ○ Clinical decision support or electronic health record interventions
	  ○ Protocols or care bundles, which may address components such as treatment agreements, urine drug screening, risk assessment, and/or naloxone prescribing
	• Interventions focused on clinical knowledge, expertise, and behavior related to prescribed or ordered opioids:
	  ○ Clinician education or academic detailing
	  ○ Clinical pharmacist consultation
	  ○ Increased access/emphasis on nonopioid or multimodal analgesia, and/or limits on opioid prescribing/ordering
	  ○ Healthcare organization guidelines
	• Interventions focused on patient and family education or engagement related to use of prescribed or ordered opioids
	• Interventions focused on tracking, monitoring, and reporting performance data related to prescribed or ordered opioids:
	  ○ Clinical audits
	  ○ Dashboards
	• Interventions focused on clinical accountability related to prescribed or ordered opioids:
	  ○ Prescriber feedback
	  ○ Peer comparison
	• Multicomponent interventions focused on opioid stewardship
		• Interventions focused on treatment of opioid use disorder (we note that this is often included in opioid stewardship interventions, but this was a separate topic in MHS III)[6]
		• Interventions or policies established by entities other than healthcare providers, including:
		  ○ Insurance company restrictions (e.g., limits on pill numbers or prior authorization)
		  ○ Government restrictions or regulations (e.g., establishment of prescription drug monitoring programs)
		  ○ Naloxone distribution outside healthcare settings (e.g., by county health departments)

Comparator	Usual care	No comparison group

Study Parameter	Inclusion Criteria	Exclusion Criteria

Outcome	Primary outcomes of interest are clinical outcomes. Secondary outcomes of interest are prescribing/ordering outcomes and process outcomes, if they are reported in studies that also report clinical outcomes.
	
	• Clinical outcomes:
	  ○ Healthcare utilization (focusing on emergency department use and hospitalizations for adverse events)
	  ○ Overdose rates (which may be relevant to inpatient opioid ordering, number of pills or doses prescribed at discharge, and long-term, chronic opioid use)
	  ○ Adverse consequences:
	  ▪ Patient-reported outcomes – changes in pain intensity or distress
	  ▪ Rates of opioid refill requests
	  ▪ Patient satisfaction
	
	• Opioid prescribing or ordering outcomes:
	  ○ Rates of opioid prescribing or ordering
	  ○ Total morphine milligram equivalents per prescription or per patient
	  ○ Number of pills per prescription
	  ○ Rates of nonopioid analgesic prescribing
	
	• Changes in process outcomes:
	  ○ Urine drug screen ordering or administration
	  ○ Treatment agreement use
	  ○ Risk assessment screening tool use
	  ○ Use of prescription drug monitoring program reports
	  ○ Other referrals relevant to pain management (behavioral health, physical therapy, etc.)
	  ○ Pain management documentation
	
	• Implementation outcomes (Review Questions 6 and 7)
	  ○ Barriers and facilitators
	  ○ Cost, staffing, time
		Studies with prescribing/ordering outcomes or process outcomes or implementation outcomes without clinical outcomes

Timing	• Systematic reviews published since 2019 • Original studies published since 2016, the year the initial CDC guideline on opioid prescribing was published, which may have led to shifts in prescribing	• Systematic reviews published before 2019 • Original studies published before 2016
Setting	Healthcare settings in the United States	• Outside of healthcare (e.g., State-level regulation) • Nursing home or prison settings • No site in the United States

Study Parameter	Inclusion Criteria	Exclusion Criteria
Type of studies	• Systematic reviews • Randomized controlled trials, nonrandomized controlled trials, and observational studies with a comparison group • Studies should include at least 50 pills, prescriptions, or patients or at least 50 clinicians, to ensure a minimum number to limit studies with too small of a sample size to provide meaningful results	• Narrative reviews, scoping reviews, editorials, commentaries, and abstracts • Qualitative studies without quantitative data

CDC = Centers for Disease Control and Prevention; MHS = Making Healthcare Safer; PSP = patient safety practice

2.2 Literature Searches for Studies of Effectiveness

We searched PubMed and the Cochrane Library, supplemented by a narrowly focused search for unpublished reports that are publicly available from governmental agencies, professional societies, or membership organizations with a strong interest in the topic, including the Centers for Disease Control and Prevention (CDC), AHRQ, the National Institutes of Health (NIH), National Quality Forum (NQF), and American Hospital Association (AHA). Given that MHS III used such a limited search, rather than using the end of that report as the start date for our search, we searched for original studies since the release of the CDC guidelines in 2016 that contributed to changes in practice and opioid stewardship interventions, and we searched through April 2023. For details of the search strategy, see Appendix A.

2.3 Data Extraction (Selecting and Coding)

We used the AI feature of DistillerSR (AI Classifier Manager) as a semi-automated screening tool to conduct this review efficiently at the title and abstract screening stage. The title and abstract of each citation were screened by a team member based on predefined eligibility criteria (Table 1). The screening responses by the team members were used to teach the AI Classifier Manager, which served as a second reviewer of each citation. Discrepancies between team members and the AI Classifier Manager were reviewed and resolved by the team members. The full text of each remaining potentially eligible article was reviewed by a single team member to confirm eligibility. A second team member checked a 10 percent sample of the full text reviews to verify that important studies were not excluded.

We prioritized our efforts by extracting detailed information from the highest quality studies. Given the large number of systematic reviews and studies with strong designs, we focused on extracting detailed information from systematic reviews, randomized controlled trials (RCTs), nonrandomized controlled trials (NRCTs), and observational studies with a comparison group. We listed relevant studies having weak pre-post designs with limited information in Appendix C, but we did not synthesize them in the text of the results section.

Reviewers extracted available information and organized it according to the review questions and included author, year, study design, frequency and severity of the harms, measures of harm, characteristics of the PSP, rationale for the PSP, outcomes, implementation barriers and facilitators, resources needed for implementation, and description of toolkits. One reviewer completed the data abstraction, and a second reviewer checked the first reviewer's abstraction for completeness and accuracy.

2.4 Risk of Bias (Quality) Assessment

For studies that addressed Review Question 5 about the effectiveness of PSPs, we used the Cochrane Collaboration's tool for assessing the risk of bias of RCTs or the

ROBINS-I tool for assessing the Risk Of Bias In Non-randomized Studies – of Interventions.[10,11] We did not assess the risk of bias in the pre-post studies, recognizing that they have a high risk of bias because of the lack of a separate comparison group.

For RCTs, we used the items in the Cochrane Collaboration's tool that cover the domains of selection bias, performance bias, detection bias, attrition bias, reporting bias, and other bias.[10] For nonrandomized studies, we used specific items in the ROBINS-I tool that assess bias due to confounding, bias in selection of participants into the study, bias in classification of interventions, bias due to deviations from intended interventions, bias due to missing data, bias in measurement of outcomes, and bias in selection of the reported results. The risk of bias assessments focused on the main outcome of interest in each study.[11]

For a recent eligible systematic review, the primary reviewer used the criteria developed by the United States Preventive Services Task Force Methods Workgroup for assessing the quality of systematic reviews.[12]

- Good - Recent relevant review with comprehensive sources and search strategies; explicit and relevant selection criteria; standard appraisal of included studies; and valid conclusions.
- Fair - Recent relevant review that is not clearly biased but lacks comprehensive sources and search strategies.
- Poor - Outdated, irrelevant, or biased review without systematic search for studies, explicit selection criteria, or standard appraisal of studies.

2.5 Strategy for Data Synthesis

We narratively summarized findings across systematic reviews and across primary studies. We did not conduct a meta-analysis. For Review Question 5 about the effectiveness of PSPs, we recorded information about the context of each primary study and whether the effectiveness of the PSP differed across patient subgroups. As the systematic reviews generally summarized the literature descriptively and did not grade the strength of evidence, we based our grading on the primary studies. We graded the strength of evidence for PSPs with more than one primary study of effectiveness using the methods outlined in the AHRQ Effective Health Care Program Methods Guide for Effectiveness and Comparative Effectiveness Reviews and focusing on the key clinical outcome for each intervention type such as adverse consequences of changes in pain intensity or healthcare utilization, and the key opioid prescribing outcome such as quantity or doses.[13]

3. Evidence Summary

3.1 Benefits and Harms

- PSPs involving clinical decision support or electronic health record interventions, and multicomponent PSPs (including for chronic pain) were associated with decreases in opioid prescribing or doses (low strength of evidence).
- PSPs involving patient engagement and education had mixed results for opioid prescribing outcomes (insufficient strength of evidence).
- PSPs involving clinical decision support or electronic health record interventions, patient engagement and education, and multicomponent PSPs did not show an increase in pain, emergency department visits, or hospitalizations (low strength of evidence for all outcomes).
- The evidence was insufficient on the following intervention types: opioid stewardship committees, protocols or care bundles, clinician education or academic detailing, clinical pharmacist consultation, increased access/emphasis on nonopioid or multimodal analgesia, and/or limits on opioid prescribing/ordering, healthcare organization guidelines, clinical audits, dashboards, prescriber feedback, and peer comparison
- The evidence was insufficient on outcomes of opioid refill requests and refills, patient satisfaction, or overdose.
- Barriers included lack of clinician training, workload, gaps in communication, and inadequate access to non-pharmacological resources. Clinician and patient acceptance of intervention components were facilitators.

3.2 Future Research Needs

- More research is needed on opioid stewardship committees, dashboards and peer comparisons, and care bundle interventions such as urine drug testing, drug use contracts, and prescription drug monitoring program queries, which are commonly used health system interventions and quality indicators.

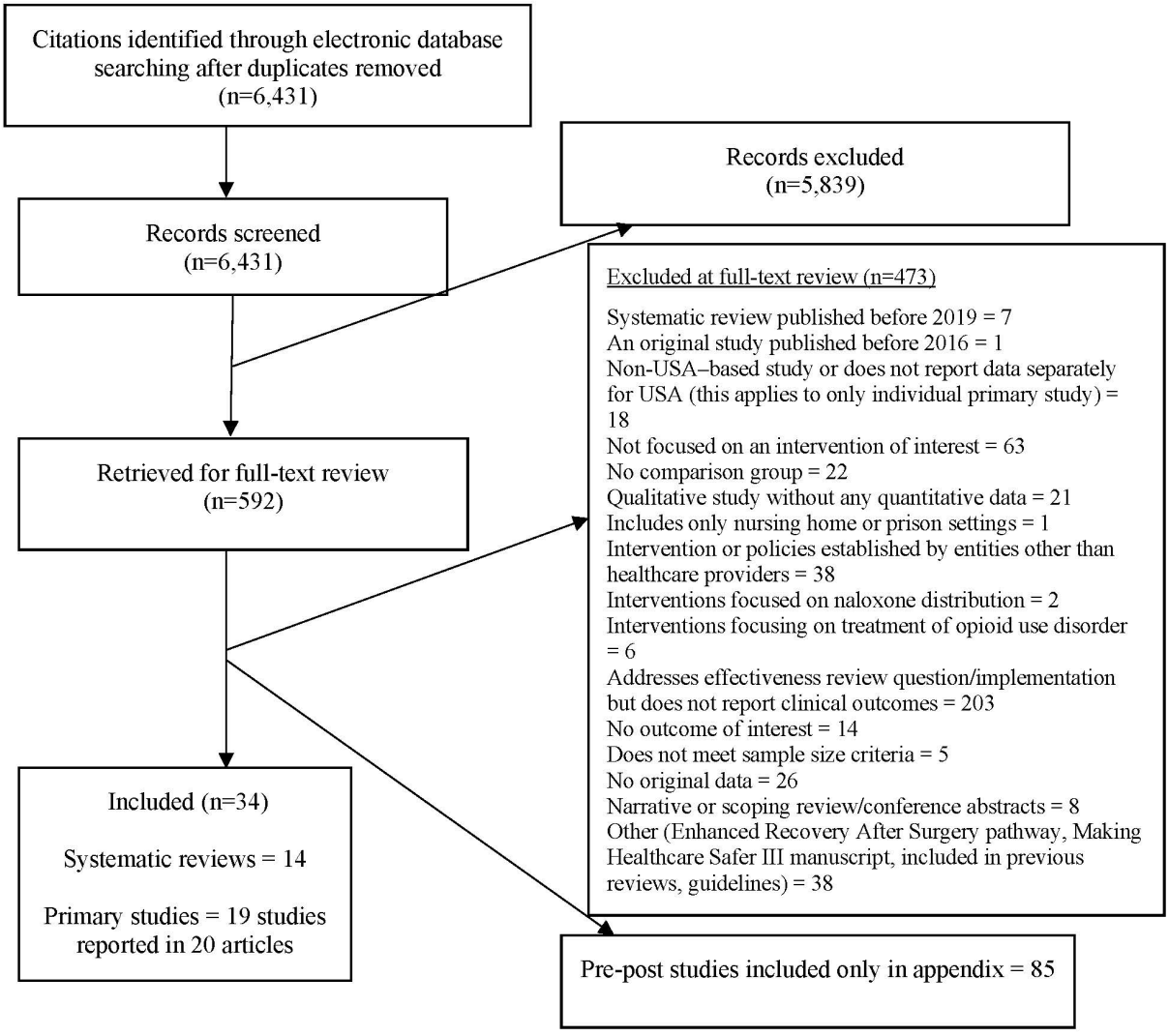
4. Evidence Base

4.1 Number of Studies

Our search retrieved 6431 unique titles and abstracts from which we reviewed 6431 full text articles for eligibility (Figure 1). We found 34 studies that met our eligibility criteria. A listing of studies excluded during full text review is included in Appendix B, List of Included Studies, and information abstracted from each included study is provided in Appendix C, Evidence Tables.

Pre-post studies do not have a separate comparison group and thus have a high risk of bias, we did not discuss them in the main body of the report, but we summarize them briefly in the appendix.

Figure 1. Results of the search and screening

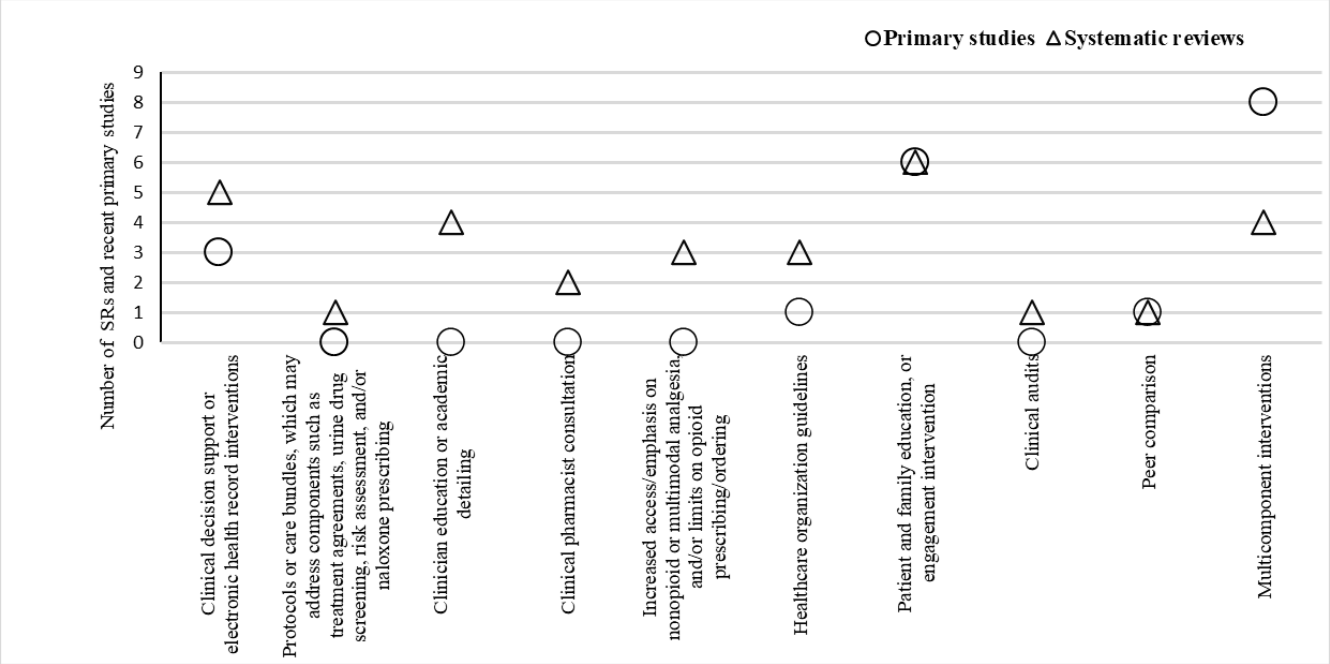


4.2 Findings for Review Questions

Figure 2 presents an overview of included evidence by type of opioid stewardship intervention. We did not find any recent systematic reviews or original studies that specifically examined the effectiveness of opioid stewardship committees, dashboards, or prescriber feedback.

Characteristics of the included systematic reviews and primary studies are presented in Tables 2a and 2b.

Figure 2. Overview of included evidence by type of opioid stewardship intervention*†



SR = systematic review

* The numbers of pre-post studies are not included in this figure.

†Primary studies and systematic review references are available in Table 3.

Table 2a. Characteristics of the included systematic reviews

Author, Year	Objective	Search Date Included Studies, n Study Designs, n	Opioid Stewardship Interventions	Outcomes of Interest	Quality of the Review*
Avery, 2022[14]	Review interventions to reduce long-term opioid treatment in people with chronic noncancer pain.	Search date: July 2021 Included studies, 36 RCTs = 27 NRCTs = 5 Observational = 0 Other = 4	• Interventions addressing clinical knowledge, expertise, and behavior • Patient and family education or engagement	• Pain intensity or distress • Rates of opioid prescribing or ordering • Total MME per prescription or per patient	Good

Author, Year	Objective	Search Date Included Studies, n Study Designs, n	Opioid Stewardship Interventions	Outcomes of Interest	Quality of the Review*
Carnes, 2022[15]	Review of the effectiveness of various types of interventions in reducing opioid prescriptions after urological surgery.	Search date: January 2000 to January 2021 Included studies, 22 RCTs = 0 NRCTs = 0 Observational = 22 Other = 0	• Studies individually addressing different types of interventions were combined in the synthesis	• Healthcare utilization • Opioid refill requests • Pain intensity or distress • Patient satisfaction • Rates of opioid prescribing or ordering	Fair
Haegerich, 2019[16]	Synthesizes effectiveness of prevention strategies that address prescription and illicit opioid overdose.	Search date: January 2013 to May 2018 Included studies, 251 RCTs = 32 NRCTs = 5 Observational = 155 Other = 59	• Interventions addressing clinical knowledge, expertise, and behavior • Organizational leadership and policies • Patient and family education or engagement • Tracking, monitoring, and reporting performance data • Multicomponent interventions (system policies such as opioid dosing limits plus education)†	• Healthcare utilization • Pain intensity or distress • Number of pills per prescription • Overdose rates • Rates of opioid prescribing or ordering • Total MME per prescription or per patient	Good
Hopkins, 2019[17]	Identify the objective impacts of education interventions on opioid prescribing in the acute care setting.	Search date: December 2018 Included studies, 9 RCTs = 0 NRCTs = 0 Observational = 9 Other = 0	• Interventions addressing clinical knowledge, expertise, and behavior	• Opioid refill requests • Pain intensity or distress • Number of pills per prescription • Rates of nonopioid analgesic prescribing • Rates of opioid prescribing or ordering • Total MME per prescription or per patient	Fair
Iqbal, 2022[18]	Assess the effectiveness of interventions delivered by pharmacists in outpatient clinical settings, community pharmacies and primary care	Search date: January 1990 to June 2020 Included studies, 14 RCTs = 1 NRCTs = 2	• Interventions addressing clinical knowledge, expertise, and behavior	• Pain intensity or distress • Other referrals relevant to pain management • Rates of nonopioid analgesic prescribing • Total MME per prescription or per patient	Fair

Author, Year	Objective	Search Date Included Studies, n Study Designs, n	Opioid Stewardship Interventions	Outcomes of Interest	Quality of the Review*
	services in optimizing opioid therapy for people with chronic nonmalignant pain. Explore stakeholders' opinions about role of pharmacists in optimizing opioid therapy.	Observational = 8 Other = 3			
Kadakia, 2020[19]	Evaluate the impact of prescription opioid-related education provided to a patient by a healthcare provider on patient outcomes.	Search date: 1996 to October 2018 Included studies, 10 [study design was not reported]	• Patient and family education or engagement	• Pain intensity or distress • Overdose rates • Total MME per prescription or per patient	Poor‡
Langford, 2023[20]	Synthesize and evaluate evidence from systematic reviews examining the effectiveness and outcomes of patient-targeted opioid deprescribing interventions for all types of pain.	Search date: August 2011 to August 2021 Included studies, 12 RCTs = 0 NRCTs = 0 Observational = 0 Other = 12	• Multicomponent interventions†	• Rates of opioid prescribing or ordering • Pain intensity or distress	NA§
Liu, 2020[21]	Summarize the effectiveness of interventions on appropriate opioid use for noncancer pain among hospital inpatients.	Search date: 1960 to March 2018 Included studies, 37 RCTs = 4 NRCTs = 0 Observational = 31 Other = 2	• Interventions addressing clinical knowledge, expertise, and behavior • Organizational leadership and policies • Tracking, monitoring, and reporting performance data	• Healthcare utilization • Pain intensity or distress • Patient satisfaction • Rates of nonopioid analgesic prescribing • Rates of opioid prescribing or ordering	Fair
Lovecchio, 2019[22]	Evaluate institutional strategies that reduce opioid administration or consumption after orthopedic surgery.	Search date: October 2018 Included studies, 13 RCTs = 1 NRCTs = 0 Observational = 11 Other = 1	• Interventions addressing clinical knowledge, expertise, and behavior • Organizational leadership and policies • Patient and family education or engagement	• Opioid refill requests • Pain intensity or distress • Patient satisfaction • Rates of nonopioid analgesic prescribing • Rates of opioid prescribing or ordering • Total MME per prescription or per patient	Fair

Author, Year	Objective	Search Date Included Studies, n Study Designs, n	Opioid Stewardship Interventions	Outcomes of Interest	Quality of the Review*
Phinn, 2023[23]	Summarize the effectiveness of organizational interventions on appropriate opioid prescribing for noncancer pain upon hospital discharge.	Search date: 2011 to March 2021 Included studies, 43 RCTs = 3 NRCTs = 0 Observational = 38 Other = 2	• Interventions addressing clinical knowledge, expertise, and behavior • Multicomponent interventions† • Organizational leadership and policies	• Healthcare utilization • Pain intensity or distress • Patient satisfaction • Rates of nonopioid analgesic prescribing • Rates of opioid prescribing or ordering	Fair
Raoul, 2022[24]	Review and analyze interventions designed to reduce the rate of opioid prescriptions or the quantity prescribed for pain in adults discharged from the emergency department.	Search date: May 15, 2020 Included studies, 63 RCTs = 1 NRCTs = 0 Observational = 39 Other = 23	• Interventions addressing clinical accountability • Clinical knowledge, expertise, and behavior • Organizational leadership and policies • Tracking, monitoring, and reporting performance data	• Patient satisfaction • Rates of opioid prescribing or ordering • Total MME per prescription or per patient	Poor‡
Wong, 2020[25]	Synthesize the available evidence on interventional strategies to improve care-associated outcomes for patients with chronic noncancer pain who frequently use the emergency department.	Search date: June 2018 Included studies, 13 RCTs = 4 NRCTs = 0 Observational = 9 Other = NR	• This synthesis combined studies of different types of interventions (e.g., care policies, care plans, care coordination)	• Healthcare utilization • Total MME per prescription or per patient	Fair
Zhang, 2020[26]	Summarize strategies to reduce postsurgical opioid prescribing at discharge.	Search date: December 2018 Included studies, 24 RCTs = 1 NRCTs = 0 Observational = 22 Other = 1	• Interventions addressing clinical knowledge, expertise, and behavior • Organizational leadership and policies • Patient and family education or engagement	• Healthcare utilization • Opioid refill requests • Pain intensity or distress • Number of pills per prescription • Patient satisfaction • Rates of opioid prescribing or ordering • Total MME per prescription or per patient	Fair
Zorrilla-Vaca, 2022[27]	Evaluate the impact of perioperative opioid education on postoperative opioid consumption	Search date: September 2020 Included studies, 11	• Patient and family education or engagement	• Opioid refill requests	Good

Author, Year	Objective	Search Date Included Studies, n Study Designs, n	Opioid Stewardship Interventions	Outcomes of Interest	Quality of the Review*
	patterns including opioid cessation, number of pills consumed, and opioid prescription refills.	RCTs = 11 NRCTs = 0 Observational = 0 Other = NR			

MME = morphine milligram equivalents; n = sample size; NA = not applicable; NR = not reported; NRCT = nonrandomized controlled trial; RCT = randomized controlled trial

*We used the criteria developed by the United States Preventive Services Task Force Methods Workgroup for assessing the quality of systematic reviews.

†Please see Appendix C, Evidence Table C-7 for the additional details on the multicomponent intervention.

‡Systematic reviews were given a poor rating due to lack of standard study assessment such as risk of bias or strength of evidence grading or high possibility of bias in statistical methods.

§Langford, et al.[20] is a review of systematic reviews and not applicable to be assessed using the United States Preventive Services Task Force Methods Workgroup tool for assessing quality of systematic reviews.

Table 2b. Characteristics of the included primary studies (pre-post studies listed in Appendix*)

Opioid Stewardship Intervention Category	Author, Year Study Design	Study Setting Number of Participants, N	Description of Intervention	Outcomes of Interest
Organizational leadership and policies	Ahmed, 2016[28] Nonrandomized interventional study	Emergency Department N=144 patients	ED headache treatment algorithm with stepwise instructions for diagnosis, treatment, and discharge planning	• Healthcare utilization • Rates of opioid prescribing or ordering • Pain intensity or distress
	Bachhuber, 2021[29] Cluster randomized control trial	Primary care and ED N=21,331 patients	Site level change to the EHR to implement a uniform, reduced, default dispense quantity of 10 tablets for new opioid analgesics prescriptions	• Healthcare utilization • Rates of opioid prescribing or ordering • Opioid refill requests • Number of pills per prescription • Total MME per prescription or per patient
	Bachhuber., 2022[30] Cluster randomized control trial	Ambulatory care N=6,309 patients	Site-level change to the EHR to implement a uniform, reduced, default dispense quantity of 10 tablets or 5 tablets for new opioid analgesic prescriptions.	• Healthcare utilization • Rates of opioid prescribing or ordering • Opioid refill requests • Number of pills per prescription • Total MME per prescription or per patient
Clinical knowledge, expertise, and behavior related to prescribed or ordered opioids	Sada, 2019[31] Quality improvement	Ambulatory care N= 88 patients	A guideline was developed to standardize post-discharge prescribing, and the improvement process was repeated iteratively.	• Opioid refill requests • Patient dissatisfaction • Number of pills per prescription • Total MME per prescription or per patient

Opioid Stewardship Intervention Category	Author, Year Study Design	Study Setting Number of Participants, N	Description of Intervention	Outcomes of Interest
Patient and family education or engagement intervention	Syed, 2018[32] RCT	Ambulatory care N=140 patients	Formal education detailing recommended postoperative opioid usage, side effects, dependence, and addiction via a 2-minute narrated video and a handout detailing the risks of "narcotic" overuse and abuse.	• Pain intensity or distress
	Egan, 2020[33] RCT	Ambulatory care N=100 patients	Brief patient-based educational intervention using an educational instrument containing information about pain expectations and goals, examples of opioid and adjunct medications that may be used perioperatively, risks associated with opioid use and examples of non-medication pain control methods and statements to normalize the pain experience for the patient.	• Rates of opioid prescribing or ordering • Opioid refill requests • Pain intensity or distress • Total MME per prescription or per patient
	Voepel-Lewis, 2021[34] RCT	Inpatient N= 604 parent-child dyads	Routine instruction plus the Scenario-Tailored Opioid Messaging Program educational intervention, designed to provide scenario-specific opioid risk and benefit information meant to promote better decisions toward pain and ADE reduction.	• Healthcare utilization • Rates of opioid prescribing or ordering • Pain intensity or distress
	Stepan, 2021[35] RCT	Ambulatory care N= 267 patients	Standard presurgical counseling and standardized perioperative pain management education consisting of a 7-minute educational video along with a laminated card summarizing preoperative pain education distributed as part of postoperative instructions.	• Opioid refill requests • Pain intensity or distress • Number of pills per prescription • Patient satisfaction
	Delara, 2022[36] RCT	Ambulatory care N=73 women	A shared decision-making framework using a written script to guide the research staff to initiate conversation with the patient, describing the reason for opioid prescribing, common side effects and risks of taking opioids, and recommended management of pain. Using this framework, patients	• Healthcare utilization • Opioid refill requests • Number of pills per prescription • Patient satisfaction

Opioid Stewardship Intervention Category	Author, Year Study Design	Study Setting Number of Participants, N	Description of Intervention	Outcomes of Interest
			provided insight into the number of opioid tablets that they felt were appropriate for their post-operative management, which was then prescribed by the research team (up to 30 tablets)	
	Long, 2022[37] Prospective, randomized, open-label, noninferiority clinical trial	Ambulatory care N=83 patients	No preoperative prescription for opioids, but patients had the option to request an oxycodone prescription of ten 5-mg tablets postoperatively	• Rates of opioid prescribing or ordering • Pain intensity or distress • Patient satisfaction • Opioid refill requests
Clinical accountability related to prescribed or ordered opioids	Minegeshi, 2022[38] RCT	Ambulatory care N=140 Veterans' Health Administration facilities (medical centers)	Policy notice including an extra paragraph stating that facilities which do not meet the target of 97% case review for high-risk patients (as identified by the Stratification Tool for Opioid Risk Mitigation [STORM] dashboard) will receive technical assistance and be required to submit an action plan to improve the case review rate	• Overdose rates
Multicomponent interventions	Neven, 2016[39] RCT	ED N=165 patients	Information-exchange-assisted citywide ED care coordination program consisting of (1) ED case manager to assist with barriers to care coordination, and (2) creation of patient-specific ED care guidelines via a multidisciplinary committee and documented in the ED information exchange system that faxed the guideline to the treating provider when patients presented to the participating ED	• Healthcare utilization • Rates of opioid prescribing or ordering
	Liebschutz, 2017[40] Cluster randomized control trial	Ambulatory care N=53 primary care clinicians	Transforming Opioid Prescribing in Primary Care intervention (nurse care management, electronic registry, academic detailing, and electronic decision tools)	• Opioid refill requests • Rates of opioid prescribing or ordering • Total MME per prescription or per patient • Treatment agreement use

Opioid Stewardship Intervention Category	Author, Year Study Design	Study Setting Number of Participants, N	Description of Intervention	Outcomes of Interest
				• Urine drug screen ordering or administration
	Samet, 2021; Colasanti, 2022[41, 42] Cluster randomized control trial	Ambulatory care N=41 clinicians; 114 patients	Targeting Effective Analgesia in Clinics for HIV intervention consisting of 3 components: (1) a nurse care manager with an IT-enabled electronic registry to manage patients; (2) opioid education and academic detailing; and (3) facilitated access to addiction specialists.	• Opioid refill requests • Pain intensity or distress • Urine drug screen ordering or administration • Treatment agreement use • Risk assessment screening tool use • Patient satisfaction
	Kasman, 2021[43] Prospective cohort	Inpatient N=54 patients	The opioid-free protocol at discharge involved interventions at 5 distinct steps: (1) preoperative clinic visit, (2) preoperative surgical staging area, (3) intraoperative, (4) postanesthetic care unit, and (5) discharge	• Healthcare utilization • Rates of opioid prescribing or ordering • Pain intensity or distress • Total MME per prescription or per patient
	Vitzthum, 2022[44] Observational study with a comparison group	Ambulatory care N=42,064 opioid-naive patients	Opioid Sparing Initiative: A program dashboard aggregated patient-, clinician-, and facility-level data on opioid prescribing, including high-risk prescriptions such as high daily opioid doses (defined as 100 MME) and concomitant benzodiazepine prescriptions. To guide safer prescribing, providers were alerted to prescribing patterns identified as high risk or deviated from the institutional standard of care.	• Healthcare utilization • Rates of opioid prescribing or ordering
	Morasco, 2022[45] Cluster randomized control Trial	Ambulatory care N=35 primary care clinicians; 286 patients	Improving the Safety of Opioid Therapy intervention consisting of (1) one 2-hour educational session for clinicians on patient-centered care surrounding prescription opioid adherence monitoring, (2) a nurse care manager who met with patients to	• Pain intensity or distress • Total MME per prescription or per patient

Opioid Stewardship Intervention Category	Author, Year Study Design	Study Setting Number of Participants, N	Description of Intervention	Outcomes of Interest
			provide education and rationale for screenings. The nurse care manager also provided tailored recommendations to the PCP about strategies for improving opioid safety and (3) access for the nurse case manager to an internal medicine physician with expertise in chronic pain treatment in primary care and psychologist with expertise in treating comorbid pain and substance use disorder for additional recommendations as needed.	
	Lamm, 2022[46] Prospective cohort	Inpatient N=129 patients	Opioid reduction intervention protocol included: (a) an educational component provided at the outpatient visit with the surgeon with instructions tailored to the specific procedure, as well as the American College of Surgeons Safe and Effective Pain Control After Surgery patient tool; (b) preoperative multimodal analgesia provided 1 hour prior to operation; (c) goal-directed fluid management, limited intraoperative opioid administration at the discretion of the anesthesiologist, and local anesthetic administered at incision sites; (d) postoperative elements of the protocol included limited post-anesthesia care unit administration of opioids based on pain scores (opioids only allowed for pain visual analog score > 6), discharge counseling regarding limited opioid use at home, and instructions to alternate between acetaminophen and ibuprofen every 3 hours at home for pain.	• Healthcare utilization • Pain intensity or distress • Patient satisfaction • Total MME per prescription or per patient

Opioid Stewardship Intervention Category	Author, Year Study Design	Study Setting Number of Participants, N	Description of Intervention	Outcomes of Interest
	Martinson, 2023[47] Observational study with a comparison group	Ambulatory care N=734 veterans	Primary Care Pain Education and Opioid Monitoring Program is made up of an interdisciplinary care management consult team that implements the Veteran Affairs/Department of Defense recommended guidelines for long-term opioid therapy among patients with chronic pain being managed in primary care.	• Healthcare utilization • Total MME per prescription or per patient • Urine drug screen ordering or administration • Use of prescription drug monitoring program reports • Other referrals relevant to pain management

ADE = adverse drug effects; ED = emergency department; EHR = electronic health record; HIV = Human Immunodeficiency Virus; IT = information technology; mg = milligram; MME = morphine milligram equivalents; PCP =primary care provider; RCT = randomized controlled trial;
*Please see Appendix C, Evidence Table C-50 for additional details on pre-post studies

4.2.1 Question 1. What Are the Frequency and Severity of Harms Associated With Opioid Prescribing and Ordering?

There are several categories of potential harm associated with opioids. First are those generally considered as common adverse effects related to opioid use. A systematic review supported by the Agency for Healthcare Research and Quality (AHRQ) found that opioids were associated with an increased risk of nausea, vomiting, constipation, somnolence, dizziness, and pruritis compared to placebo at short term followup, and opioids were also associated with an increased risk of discontinuation because of adverse events compared to placebo. The strength of evidence (SOE) was considered high for all these outcomes. The systematic review did not identify an interaction with higher opioid doses and risk of short-term harm, although data was limited (low SOE). Opioids were also associated with an increased risk of discontinuation due to adverse events including somnolence, nausea, constipation, vomiting and headache compared to a nonopioid at short-term followup. Higher opioid dose and long-term opioid use were also associated with endocrinologic adverse effects (e.g., testosterone deficiency) (low SOE).[48]

Other significant opioid risks include more serious adverse events such as overdose, mortality, and development of opioid use disorder. From 1999 to 2010 in the United States, both opioid prescribing ac and overdose deaths involving prescription opioids increased fourfold. Despite declines in opioid prescribing, prescription opioids remain the most commonly misused prescription drug in the United States.[3]

In the systematic review referenced above, opioid use was associated with an increased risk of opioid abuse, overdose, dependence or addiction (low SOE). Higher doses of long-term opioid use were also associated with increased risk for overdose, overdose mortality, opioid misuse, dependence or addiction (low SOE).[48]

Overdose risk was also associated with concomitant use of other medications, including benzodiazepines and gabapentinoids (low SOE). One cohort study found that long-acting opioids were associated with increased risk of all-cause mortality. Another study found higher doses of opioids were associated with a higher risk of all-cause mortality, although longer duration of use was associated with a lower risk.[48]

Some data also suggests an association between opioid use and risk of falls, risk of major trauma or road trauma injury, and risk of myocardial infarction although this data is limited (low SOE). There was no association between long-term opioid use and risk of suicide or self-harm (low SOE).[48]

4.2.2 Question 2. What Patient Safety Measures or Indicators Have Been Used To Examine the Harms Associated With Opioids Prescribed or Ordered by Clinicians?

Several quality indicators from United States organizations address harms associated with prescribed or ordered opioids. The National Commission on Quality Assurance (NCQA) has three relevant ambulatory care indicators: one on risk of continued opioid use, defined as a high quantity of prescribed opioids for new prescriptions[49]; one for use of opioids at high dosage[50]; and one for use of opioids from multiple providers.[51] The Centers for Medicare & Medicaid Services (CMS) has one relevant indicator, for the proportion of hospital encounters where patients received an opioid and suffered an adverse event requiring the administration of naloxone.[52]

The National Quality Forum (NQF) conducted a recent environmental scan funded by the United States Department of Health and Human Services reviewing additional opioid safety quality indicators from the published and gray literature.[5] The Centers for Disease Control and Prevention (CDC) also sponsored development of a set of indicators based on the 2016 opioid guidelines.[53] The domain of appropriate opioid analgesic prescribing for patients on chronic opioids include the following indicators:

- Documentation of pathology for chronic pain prescribing
- Clinic visits every three months
- Assessment of high-risk or high-dose prescribing
- Annual drug testing
- Opioid agreements
- Documentation of violations and actions taken for closer monitoring
- Consideration of nonpharmacologic interventions
- Naloxone prescribing

For new opioid prescriptions, indicators addressed use of nonopioid medications, risk assessment, appropriate prescribing consistent with the CDC

opioid guidelines, including small amounts for initial prescriptions, avoiding initial long-term or extended-release opioid prescriptions, and followup visits. Indicators for both initial and chronic visits addressed avoiding co-prescribing with benzodiazepines and reviewing prescription drug monitoring program reports. For hospitalized patients treated with opioids, indicators addressed appropriate monitoring of respiratory status and level of sedation, rates of opioid respiratory adverse events, and overdoses.

In the systematic reviews and primary studies that we reviewed, outcomes relevant to opioid patient safety were measured using a variety of balancing, outcome, and process measures. For balancing measures, studies measured unintended consequences of interventions-clinical outcomes such as pain scores, pain-related complaints or phone calls or unplanned visits, and overall satisfaction or specifically pain satisfaction. Emergency department visits and hospitalizations were measured overall or as opioid-specific occurrences. Some studies measured refill requests and others measured rates of opioid refills. A few studies measured overdose rates, serious adverse events, or mortality.

For outcome measures, studies measured prescribing or ordering outcomes such as the rate of opioid prescriptions, the number of pills prescribed or refilled, the total dose, opioid dose reduction (for chronic pain studies), and the use of nonopioid analgesics.

For process measures, studies measured process outcomes such as urine drug testing, opioid treatment agreement completion, prescription drug monitoring program reports review and achievement of guideline concordant care, and referrals to non-pharmacologic interventions, such as cognitive behavioral therapy or physical therapy.

4.2.3 Question 3. What Opioid Stewardship Patient Safety Practices (PSPs) Have Been Used To Prevent or Mitigate the Harms Associated With Prescribed or Ordered Opioids, and in What Settings Have They Been Used?

Table 3 provides an overview of the types of PSPs that have been used to prevent or mitigate the harms associated with prescribed or ordered opioids, and the settings in which they have been used.

Table 3. Overview of opioid stewardship patient safety practices and settings

Intervention Category	Intervention	Identified Evidence and Settings
Interventions focused on opioid stewardship involving organizational leadership and policies within a healthcare facility or healthcare system	Opioid stewardship committees	None
	Clinical decision support or electronic health record interventions	We identified five systematic reviews[16,21,23,24,26] and three primary studies.[28-30] These types of interventions addressed the approach of decreasing the default opioid prescribing in electronic health records in inpatient, emergency department, and primary care and dentistry settings. One study examined an algorithm for headache care in the emergency department.
	Protocols or care bundles, which may address components such as treatment agreements, urine drug screening, risk assessment, and/or naloxone prescribing	One systematic review[23] addressed protocols where opioids consumed in the hospital guided prescribing at discharge; no primary studies addressed this topic.
Interventions focused on clinical knowledge, expertise, and behavior related to prescribed or ordered opioids	Clinician education or academic detailing	We identified four systematic reviews,[16,17 22,23] generally addressing opioid prescribing at discharge, and no recent primary studies.
	Clinical pharmacist consultation	We identified two systematic reviews,[18,26] in outpatient or community pharmacy settings (mostly review of charts) and pharmacist assistance with prescriptions in postsurgical prescribing, and no recent primary studies.
	Increased access/ emphasis on nonopioid or multimodal analgesia, and/or limits on opioid prescribing/ordering	We identified three systematic reviews [14,16,26] addressing opioid replacement treatment (defined as transition to maintenance therapy and then weaning off) and deprescription methods (which may or may not include alternative pain management techniques) for chronic pain in ambulatory settings; procedures for developing coordinated recommendations for opioid prescribing; and increasing opioid-free prescribing, often with nonopioid analgesia and related patient counseling, in postoperative care. We identified no recent primary studies for this intervention category.
	Healthcare organization guidelines (about limiting the amount of opioids per prescription)	We identified three systematic reviews [22,23,26] regarding opioids and/or emphasis of nonopioid pain medications specific to surgery and hospital discharges. We found one recent primary study standardizing opioid prescribing guidelines for mastectomy care.[31]
Interventions focused on patient and family education, or engagement related to use of prescribed or ordered opioids	Patient and family education, or engagement intervention	We identified six systematic reviews[14,16,19,22,26,27] and six primary studies.[32-37] These interventions included a variety of counseling and educational interventions in different settings about pain, opioids, and alternative options, including perioperative care and chronic pain management.
Interventions focused on tracking, monitoring, and reporting performance data related to prescribed or ordered opioids	Clinical audits	We identified one systematic review[21] addressing studies of safety monitoring of patient-controlled analgesia and prescription appropriateness, and no recent primary studies.
	Dashboards	None
	Prescriber feedback	None

Intervention Category	Intervention	Identified Evidence and Settings
Interventions focused on clinical accountability related to prescribed or ordered opioids	Peer comparison	We identified one systematic review.[24] evaluating peer comparison in the emergency department and one primary study[38] comparing dashboards and notifying facilities of consequences if performance targets were not met.
Multicomponent interventions focused on opioid stewardship	Multicomponent interventions (defined in MHS III as guideline-recommended clinical interventions or processes plus implementation strategies)	We identified one overview of systematic reviews,[20] three additional systematic reviews,[16,21,23] and eight recent primary studies (reported in 9 articles).[39-47] One type of multicomponent interventions in hospital settings included elements such as system policies on opioid prescribing, workflow changes, and dashboards, in addition to prescriber or patient education. The other type of multicomponent interventions, covering the primary studies and mostly in ambulatory settings, included prescriber education, case management and improved access to alternative resources, and patient education and/or nonpharmacological pain management support.

4.2.4 Question 4. What Is the Rationale for the Opioid Stewardship Practices That Have Been Used To Prevent or Mitigate the Harms Associated With Prescribed or Ordered Opioid?

No theoretical frameworks or formal logic models for interventions were reported in any of the included reviews or primary studies. Motivations for engaging in the work included the 2016 guideline from the CDC or other national guidance to reduce opioid access.[40-42,54] Justifications for interventions included either previous pre/post studies or randomized controlled trials (RCTs) demonstrating efficacy of interventions for opioid stewardship[29,30,33,35,36,39,45] or efficacy of similar interventions for other types of care improvement projects.[33,36,40-42]

4.2.5 Question 5. What Are the Effectiveness and Unintended Effects of Opioid Stewardship Practices, and What New Evidence Has Been Published Since the Search Was Done for the Making Healthcare Safer (MHS) III Report in 2019?

The limited search in the MHS III report included one systematic review and 14 studies, two of which were RCTs, and found that the majority of studies evaluated multicomponent interventions including guideline implementation. Other studies evaluated electronic health record tools such as decision support, alerts and prescription drug monitoring program implementation, dashboards for monitoring and/or feedback, clinician education, opioid committees, and case management. The MHS III report concluded that overall, SOE for significant reductions in opioid dosage was moderate; for clinical outcomes, only two studies evaluated reduction in

overdoses, with neither having a significant effect. The systematic review included in the MHS III report (published in 2010) evaluated opioid treatment agreements and urine drug testing in chronic pain and concluded that the strength of evidence was relatively weak for reducing opioid misuse.[55] Given the limited search in MHS III, we summarize the full literature from our search from 2016 forward instead of relying on a comparison to the MHS III review.

We identified 14 systematic reviews since 2019 (1 overview of systematic reviews and 13 reviews), and 13 RCTs (reported in 14 articles), and 6 nonrandomized studies since 2016 that assessed the effectiveness and unintended effects of opioid stewardship practices. We present the findings by intervention type (Table 4). We first discuss the evidence from systematic reviews, followed by evidence from primary studies (RCTs and nonrandomized studies with a comparison group). A detailed summary of benefits and harms from included systematic reviews and primary studies is provided in Appendix C, Evidence Tables C-2 through C-9.

A list of pre-post studies is in Appendix C (see Evidence Table C-50).

Table 4. Overview of evidence by intervention type for primary studies

Intervention Category	Intervention	No. of SRs	No. of Primary Studies	Strength of Evidence* and Key Findings Based on Primary Studies
Interventions focused on opioid stewardship involving organizational leadership and policies within a healthcare facility or healthcare system	Opioid stewardship committees	0	0	Insufficient
	Clinical decision support or electronic health record interventions	5[16,21,23,24,26]	2 RCTs[29,30] 1 nonrandomized study[28]	Low • No change in healthcare utilization • Decreased opioid prescribing
	Protocols or care bundles, which may address components such as treatment agreements, urine drug screening, risk assessment, and/or naloxone prescribing	1[23]	0	Insufficient
Interventions focused on clinical knowledge, expertise, and behavior related to prescribed or ordered opioids	Clinician education or academic detailing	4[16,17,22,23]	0	Insufficient
	Clinical pharmacist consultation	2 [18,26]	0	Insufficient
	Increased access/ emphasis on nonopioid or multimodal analgesia, and/or limits on opioid prescribing/ordering	3 [14,16,26]	0	Insufficient
	Healthcare organization guidelines (about limiting the amount of opioids per prescription)	3[22,23,26]	1 nonrandomized study[31]	Insufficient

Intervention Category	Intervention	No. of SRs	No. of Primary Studies	Strength of Evidence* and Key Findings Based on Primary Studies
Interventions focused on patient and family education, or engagement related to use of prescribed or ordered opioids	Patient and family education, or engagement intervention	6[14,16,19,22,26,27]	6 RCTs[32-37]	Low • No change in pain • Mixed results for opioid prescribing
Interventions focused on tracking, monitoring, and reporting performance data related to prescribed or ordered opioids	Clinical audits	1[21]	0	Insufficient
	Dashboards	0	0	Insufficient
Interventions focused on clinical accountability related to prescribed or ordered opioids	Prescriber feedback	0	0	Insufficient
	Peer comparison	1[24]	1 RCT[38]	Insufficient
Multicomponent interventions focused on opioid stewardship	Multicomponent interventions†	4 (1 overview of SRs)[16,20,21,23]	4 RCTs (reported in 5 articles)[39-42,45] 4 nonrandomized studies[43,44,46,47]	Low • Unchanged or improved pain • Decreased opioid prescribing

RCT = randomized controlled trial; SR =systematic review

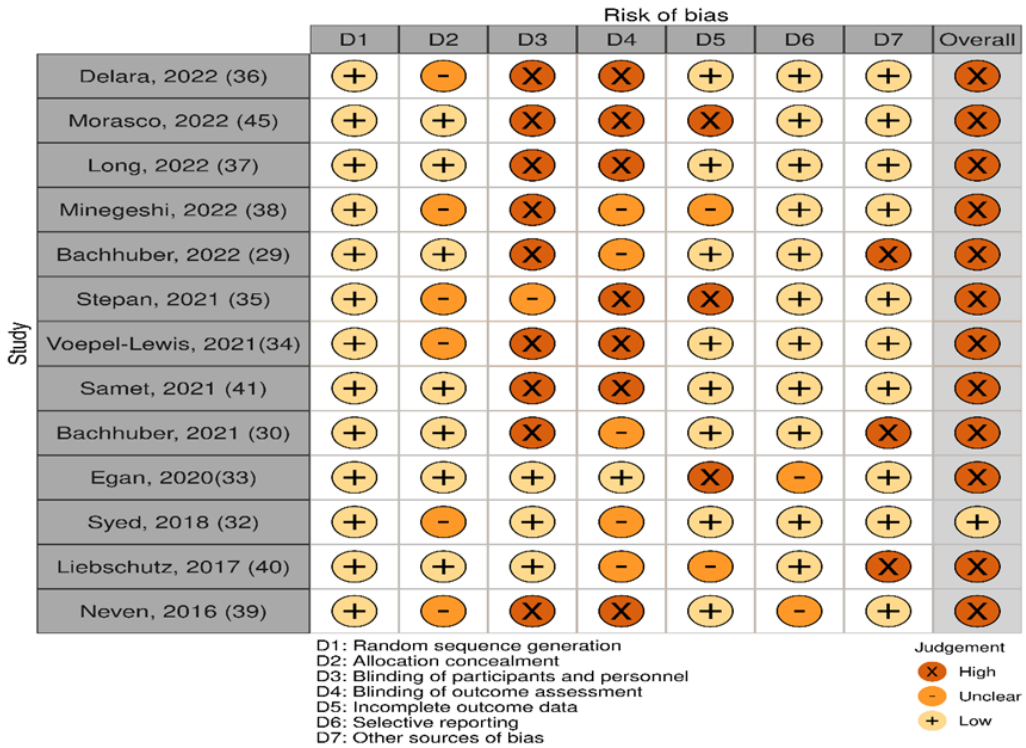
*Low strength of evidence indicates limited confidence that the estimated association lies close to the true association, and insufficient strength of evidence indicates that evidence is unavailable or does not permit a conclusion.

†Multicomponent interventions are defined as in MHS III as guideline-recommended clinical interventions or care processes plus implementation strategies.

Risk of Bias

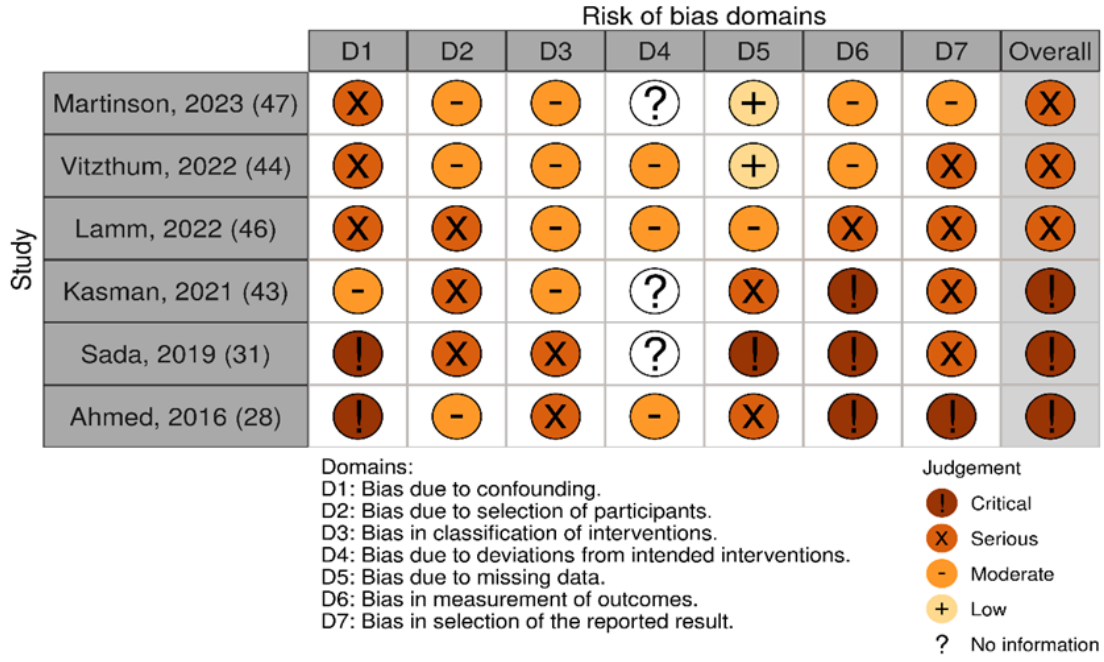
Several types of risk of bias were present in the included RCTs based on our assessments using the Cochrane Collaboration's tool.[10] The most common potential cause of bias was lack of details about allocation and blinding in the majority of studies. Twelve of the 13 RCTs had high risk of bias (Figure 3). For the nonrandomized studies, our assessments using the ROBINS-I tool (Risk Of Bias In Non-randomized Studies – of Interventions) revealed concerns for bias in confounding, patient selection, measurement of outcomes, selection of reported results, and deviations from intended assignments.[11] Five of the six nonrandomized studies had critical risk of bias (Figure 4).

Figure 3. Risk of bias assessments for randomized controlled trials included in this review*



*The figure was created using the robvis visualization tool[56]

Figure 4. Risk of bias assessments for nonrandomized studies included in this review*



*The figure was created using the robvis visualization tool[56]

4.2.5.1 Interventions Focused on Opioid Stewardship Involving Organizational Leadership and Policies Within a Healthcare Facility or Healthcare System

Intervention categories in this section include opioid stewardship committees, clinical decision support or electronic health record interventions, and protocols or care bundles.

4.2.5.1.1 Opioid Stewardship Committees

No studies met our inclusion criteria for addressing opioid stewardship committees alone.

4.2.5.1.2 Clinical Decision Support or Electronic Health Record Interventions

Five systematic reviews addressed clinical decision support or electronic health record interventions.[16,21,23,24,26] Clinical decision support at the point of care[16] and reduced default number of prescribed opioid pills in the electronic health record[23,24,26] were associated with reduced opioid prescribing. One systematic review found a significant decrease in opioid prescribing with reduced default electronic health record opioid prescribing quantity, including the finding from interrupted time series studies of a reduced rate of opioid prescription at 6 months (change -11.65; 95% confidence interval (CI): -29.30 to 5.99).[24]

Providing decision support at the point of care[16] was associated with reduced emergency department (ED) visits. Reducing the default number of opioid pills in the electronic health record[26] was not associated with a significant increase in opioid requests. A systematic review addressing computerized order entry in acute care found that its use was associated with lower rates of respiratory depression from opioids.[21] Neither of these systematic reviews graded the SOE.

We also identified two RCTs[29,30] and one nonrandomized study assessing clinical decision support or electronic health record interventions (Table 5).[28] Both RCTs compared the effect of modifying opioid prescribing defaults in the electronic health record to preexisting defaults. One RCT evaluated a default of prescribing a dispense quantity of 10 tablets compared to no change in preexisting defaults in a large health system's primary care practices and emergency departments.[29] The other RCT compared defaults of 10 tablets, 5 tablets, or no change to preexisting defaults within a health system's dentistry practices.[30] Both RCTs evaluated clinical outcomes including outpatient visits, emergency department visits, and hospitalizations during the 30-day period after the index prescription. Neither RCT found statistically significant differences in healthcare utilization.[29-30] The one RCT in dentistry practices found a statistically significant increase in opioid prescription reordering in both the 5 tablet and 10 tablet groups compared to control.[30] There was no difference in opioid prescription reorders in the second RCT based in primary care and emergency departments.[29]

Both RCTs found that the 10 tablet intervention groups (default dispense quantity) were statistically significantly more likely to have prescriptions for 10 tablets or fewer be prescribed fewer tablets at baseline and have a lower total morphine milligram equivalents (MME) per day prescribed at baseline. The RCT in the dentistry practice sustained these statistically significant differences at 30 days while the RCT in primary care and the emergency department found a statistically significant difference at 30 days in total pills prescribed but not in total MME per day. The study comparing 5 tablets to control found no differences in prescriptions for 10 tablets or fewer at baseline, number of tablets prescribed at baseline or at 30 days, nor in MME prescribed at baseline or at 30 days compared to control.

Neither RCT assessed any of the process outcomes defined in our inclusion criteria.

One nonrandomized study evaluated a treatment algorithm for headache in the ED, including diagnostic and treatment planning aids.[28] They compared patients in two post algorithm implementation periods (first six months after adoption, and then one year later) to historical controls. Compared to controls, patients in both post-implementation periods were significantly less likely to be treated with opioids or barbiturates in the emergency department or discharged with opioids or barbiturates. There were no significant differences between control and post-implementation time one (i.e., six months after algorithm implementation) groups in post-treatment pain scores, frequency of imaging, consults, or admissions. Findings were similar for post-implementation time two (i.e., one year after algorithm implementation) except for a significant increase in the number of neurology consults and admissions when compared to the control group.

We graded the SOE as low for healthcare utilization and low for opioid prescribing.

Table 5. Overview of clinical outcomes and opioid prescribing/ordering outcomes for clinical decision support or electronic health record interventions reported in the primary studies

Author, Year Study Design	Intervention Description	Opioid Prescribing Outcome at Baseline	Opioid Prescribing Outcome Post-Implementation	Pain Outcomes	Patient Satisfaction Outcomes	Healthcare Utilization Outcomes
Bachhuber, 2021[29] Cluster randomized control trial	Site level change to the EHR to implement a uniform, reduced, default dispense quantity of 10 tablets for new opioid analgesics prescriptions	**Dispense quantity <= 10 tablets, adjusted difference in differences (95% CI)** Result=7.6 (6.1 to 9.2) percentage points, p < 0.001 **Tablets prescribed, adjusted difference in differences (95% CI)** Result=-2.1 (-3.3 to -0.9), p < 0.001 **MME prescribed, adjusted difference in differences (95% CI)** Result=-14.6 (-22.6 to -6.6), p < 0.001	**Opioid analgesic prescription reorder during the 30-d period after the index prescription, adjusted difference in differences (95% CI)** Result=0.5 (-0.7 to 1.8) percentage points, p=0.4 **Total tablets prescribed during the 30-d period after the index prescription, adjusted difference in differences (95% CI)** Result=-2.7 (-4.8 to -0.6), p=0.01 **Total MME prescribed during the 30-d period after the index prescription, adjusted difference in differences (95% CI)** Result=-15.8 (-33.8 to 2.2), p=0.09	NR	NR	**Outpatient visit during the 30-day period after the index prescription, adjusted difference in differences (95% CI)** Result=-0.7 (-1.6 to 0.2) percentage points, p=0.13 **ED visit during the 30-day period after the index prescription, adjusted difference in differences (95% CI)** Result= 0.1 (-0.2 to 0.4) percentage points, p > 0.47 **Hospitalization during the 30-day period after the index prescription, adjusted difference in differences (95% CI)** Result=0.2 (-0.08 to 0.4) percentage points, p=0.18
Bachhuber, 2022[30] Cluster randomized trial	Site-level change to the EHR to implement a uniform, reduced, default dispense quantity of 10 tablets or 5 tablets for new opioid analgesic prescriptions	**10 Tablet Default Site vs Control** **Dispense quantity <= 10 tablets, adjusted difference in differences (95% CI)** Result=38.7 (11.5 to 66) percentage points, p=0.003 **Tablets prescribed, adjusted difference in differences (95% CI)**	**10 Tablet Default Site vs Control** **Opioid analgesic prescription reorder during the 30-day period after the index prescription, adjusted difference in differences (95% CI)** Result=3.3 (0.2 to 6.4) percentage points, p=0.04	NR	NR	**10 Tablet Default Site vs Control** **Outpatient visit during the 30-day period after the index prescription, adjusted difference in differences (95% CI)** Result=3.4 (-0.2 to 7) percentage points, p=0.08 **ED visit during the 30-day period after the index prescription,**

Author, Year Study Design	Intervention Description	Opioid Prescribing Outcome at Baseline	Opioid Prescribing Outcome Post-Implementation	Pain Outcomes	Patient Satisfaction Outcomes	Healthcare Utilization Outcomes
		Result=-3.3 (-5.9 to -0.7), p=0.01 **MME prescribed, adjusted difference in differences (95% CI)** Result=-14.1 (-27.8 to -0.4), p=0.04 **5 Tablet Default Site vs Control** **Dispense quantity <= 10 tablets, adjusted difference in differences (95% CI)** Result=0.1 (-5.8 to 6.1) percentage points, p=0.97 **Tablets prescribed, adjusted difference in differences (95% CI)** Result=-0.2 (-0.7 to 0.2), p=0.26 **MME prescribed, adjusted difference in differences (95% CI)** Result=2.4 (-1.4 to 6.2), p=0.22	**Total tablets prescribed during the 30-day period after the index prescription, adjusted difference in differences (95% CI)** Result=-3.3 (-5.6 to -1), p=0.002 **Total MME prescribed during the 30-day period after the index prescription, adjusted difference in differences (95% CI)** Result=-15.7 (-28.1 to -3.3), p=0.008 **5 Tablet Default Site vs Control** **Opioid analgesic prescription reorder during the 30-day period after the index prescription, adjusted difference in differences (95% CI)** Result=2.6 (0.2 to 4.9) percentage points, p=0.03 **Total tablets prescribed during the 30-day period after the index prescription, adjusted difference in differences (95% CI)** Result=0.1 (-0.7 to 0.9), p=0.85 **Total MME prescribed during the 30-day period after the index prescription, adjusted**			**adjusted difference in differences (95% CI)** Result= 0.6 (-0.2 to 1.4) percentage points, p=0.16 **Hospitalization during the 30-day period after the index prescription, adjusted difference in differences (95% CI)** Result=0.1 (-0.8 to 0.9) percentage points, p=0.84 **5 Tablet Default Site vs Control** **Outpatient visit during the 30-day period after the index prescription, adjusted difference in differences (95% CI)** Result=1.7 (-0.7 to 4.2) percentage points, p=0.16 **ED visit during the 30-day period after the index prescription, adjusted difference in differences (95% CI)** Result= 0.7 (-0.3 to 1.6) percentage points, p=0.26 **Hospitalization during the 30-day period after the index prescription, adjusted difference in differences (95% CI)** Result=0.4 (-0.5 to 1.3) percentage points, p=0.64

Author, Year Study Design	Intervention Description	Opioid Prescribing Outcome at Baseline	Opioid Prescribing Outcome Post-Implementation	Pain Outcomes	Patient Satisfaction Outcomes	Healthcare Utilization Outcomes
			difference in differences (95% CI) Result=3.1 (-5.1 to 11.2), p=0.46			
Ahmed, 2016[28] Nonrandomized interventional study	ED headache treatment algorithm with stepwise instructions for diagnosis, treatment, and discharge planning		**Control vs Implementation Time 1** Number of patients treated with opioids or barbiturates (%) Result=33 (66%) (control) vs 3 (6.8%) (intervention), p < 0.001 Number of patients discharged with opioids or barbiturates (%) Result=17 (37) (control) vs 5 (12.2) (intervention), p=0.08 **Control vs Implementation Time 2** Number of patients treated with opioids or barbiturates (%) Result=33 (66%) (control) vs 14 (28%) (intervention), p < 0.001 Number of patients discharged with opioids or barbiturates (%) Result=17 (37) (control) vs 2 (6) (intervention), p=0.02	**Control vs Implementation Time 1** Mean pre-treatment pain score (0 –10) (SD) Result=8.4 (+/- 1.64) (control) vs 7.5 (+/- 2.41) (intervention), p=0.04 Mean post-treatment pain score (0-10) (SD) Result=3.9 (+/- 0.46) (control) vs 3.2 (+/- 0.4) (intervention), p=0.24 **Control vs Implementation Time 2** Mean pre-treatment pain score (0-10) (SD) Result=8.4 (+/- 1.64) (control) vs 8.6 (+/- 1.68) (intervention), p=0.63 Mean post-treatment pain score (0-10) (SD) Result=3.9 (+/- 0.46) (control) vs 3.7 (+/-	NR	**Control vs Implementation Time 1** No. of patients who underwent imaging (%) Result=25 (50) (control) vs 24 (55) (intervention), p=0.66 No. of consults (%) Result=3 (6) (control) vs 3 (6.8) (intervention), p=0.8 No. of admissions (%) Result=4 (8) (control) vs 3 (6.8) (intervention), p=0.83 No. with follow up appointment (%) Result=27 (54) (control) vs 40 (97.5) (intervention), p < 0.001 **Control vs Implementation Time 2** No. imaged (%) Result=25 (50) (control) vs 20 (40) (intervention), p=0.32 No. of consults (%) Result=3 (6) (control) vs 17 (34) (intervention), p=0.001 No. of admissions (%)

Author, Year Study Design	Intervention Description	Opioid Prescribing Outcome at Baseline	Opioid Prescribing Outcome Post-Implementation	Pain Outcomes	Patient Satisfaction Outcomes	Healthcare Utilization Outcomes
				0.48) (intervention), p=0.69		Result=4 (8) (control) vs 17 (34) (intervention), p=0.001 No. with follow up appointment (%) Result=27 (54) (control) vs 11 (73) (intervention), p=0.018

CI = confidence interval; ED = emergency department; MME =morphine milligram equivalents; no. =number; SD = standard deviation; vs =versus

4.2.5.1.3 Protocols or Care Bundles (Which May Address Components Such as Treatment Agreements, Urine Drug Screening, Risk Assessment, and/or Naloxone Prescribing)

One systematic review assessed protocols that used the amount of prescribed opioids used for hospitalized patients to guide discharge prescribing.[23] This review found that the protocols resulted in reduced quantities of opioid prescribed at discharge. We did not identify any systematic reviews or recent primary studies addressing care bundles.

4.2.5.2 Interventions Focused on Clinical Knowledge, Expertise, and Behavior Related to Prescribed or Ordered Opioids

Intervention categories in this section include clinician education or academic detailing, clinical pharmacist consultation, increased access/emphasis on nonopioid or multimodal analgesia and/or limits on opioid prescribing/ordering, and healthcare organization guidelines.

4.2.5.2.1 Clinician Education or Academic Detailing

Four systematic reviews addressed clinician education or academic detailing alone.[16,17,22,23] Three of these reviews reported an association with reduced opioid prescribing after the intervention.[16,17,23] For clinical outcomes, systematic reviews did not find an increase in refill requests,[17] or pain-related complaints,[17] but found an increase in number of patients returning to the emergency department within 30 days for pain control.[23] Only one of the systematic reviews graded the quality of evidence, and determined it to be low for a group of interventions that included this category.[16]

4.2.5.2.2 Clinical Pharmacist Consultation

Two systematic reviews addressed clinical pharmacist consultation.[18,26] The interventions addressed clinical pharmacist interventions in outpatient or community pharmacy settings (mostly review of charts)[18] and pharmacist assistance with prescriptions in postsurgical prescribing.[26] Both reviews found an overall reduction in overall opioid dose after pharmacist intervention[18,26] and one study included in this review found an increase in nonopioid analgesics.[18]

For clinical outcomes, one review found that 5 of 8 studies showed significant reduction in pain intensity[18] and the other review found no increase in post-operative pain,[26] and no increases in hospital visits.[26]

For process outcomes, one study found an increase in physical therapy referrals.[18]

Neither of these systematic reviews graded the SOE.

4.2.5.2.3 Increased Access/ Emphasis on Nonopioid or Multimodal Analgesia and/or Limits on Opioid Prescribing/Ordering

We identified three systematic reviews addressing this type of intervention.[14,16,26] These reviews found that opioid replacement treatment (defined as transition to maintenance therapy with a different opioid and then attempting to taper down the opioid) showed no significant difference for opioid dose.[14] The reviews also found that deprescribing methods in ambulatory chronic pain (with or without nonopioid pain management techniques), coordinated recommendations for opioid prescribing, and increasing opioid-free prescribing (often with nonopioid analgesia and related patient counseling) all reduced opioid dose or prescribing.[14,16,26] The review on opioid-free prescribing found results for clinical outcomes, with no differences in pain, requirement for additional prescriptions, or satisfaction.[26] One of these reviews graded the SOE and found moderate level certainty for the outcome of opioid dose reduction based on a single study.

4.2.5.2.4 Healthcare Organization Guidelines

Three systematic reviews addressed healthcare organization guidelines for opioids and/or emphasizing nonopioid pain medications in surgical or hospital discharge.[22,23,26] All three found decreases in prescription size and doses.[22,23] For clinical outcomes, there was generally improvement in pain, no difference in patient satisfaction or phone calls for uncontrolled pain, and mixed results for refills or requests.[22,23,26]

We identified one primary study of a quality improvement project assessing patient use of post-operative medications; patient satisfaction with their pain management; and standardizing opioid prescribing guidelines for patients undergoing mastectomy with immediate reconstruction.[31] Across the phases, the overall amount of opioids prescribed per patient was reduced (median of 450 MMEs per day in Phase I, and 98 MMEs per day in Phase IV). The range of the amount of prescribed opioids across patients was reduced from the beginning to end of the project (225 to 925 MMEs per day in Phase I, and 0 to 250 MMEs per day in Phase IV). Across phases, patient satisfaction fluctuated, starting at 93% of patients reporting high satisfaction in Phase I (baseline), 83% in Phase II, 73% in Phase III, and 93% in Phase IV.

We determined that the SOE was insufficient.

4.2.5.3 Interventions Focused on Patient and Family Education or Engagement Related to Use of Prescribed or Ordered Opioids

Six systematic reviews addressed patient and family education or engagement interventions.[14,16,19,22,26,27] Specific interventions included a variety of counseling and educational interventions in different settings, including perioperative care and chronic pain management, and pain self-management and tapering down opioids.

Four of the five reviews that addressed opioid dose prescribing found significantly reduced doses or discontinued therapy;[14,16,22,26] the other review found no difference in a single study.[19] All of the five systematic reviews addressing pain found reductions in pain intensity[14,16,19,22,26] and the one review that addressed opioid refill requests found no difference, with low level of certainty.[27] One systematic review focusing on long-term management of chronic pain[14] found that patient and family education or engagement interventions that included pain self-management with tapering down opioids moderately reduced opioid dose (mean difference in MME per day –14.31 (95% CI, –21.57 to –7.05) compared to no intervention, with moderate level of certainty. The review found a moderate effect on pain intensity (standardized mean difference –0.59 (95% CI, –1.02 to –0.16), with low level of certainty).

We identified six RCTs that addressed patient and family education or engagement intervention. We report the findings from these six RCTs by outcomes below (Table 6).

4.2.5.3.1 Clinical Outcomes

Six RCTs assessed the effect of patient and family education or engagement on clinical outcomes (Table 6).[32-37] In general, RCTs evaluated education-related interventions (such as pain expectations, use of opioids for pain including risks, and the use of nonopioid analgesics) compared to previously established standard of care perioperative education or counseling. Two studies included a shared decision-making model which incorporated patient expectations of how many opioid tablets they believe they should receive after surgery in subsequent prescribing.[36,37] All studies were conducted in the ambulatory surgery setting. All six RCTs assessed multiple clinical outcomes including pain, patient satisfaction, healthcare utilization, and opioid refill requests (Table 6).

Five of the six RCTs assessed pain as a clinical outcome.[32-35,37] Four of the RCTs found no statistically significant differences in pain between groups.

One RCT compared opioid related postoperative education to standard of care in patients undergoing primary arthroscopic rotator cuff repair.[32] They found statistically significantly lower pain scores in the study group compared to the control group at 2 weeks and 6 weeks, with no significant difference at 3 months.

Four of the RCTs evaluated opioid refills.[33,35-37] One RCT in patients undergoing ambulatory hand surgery found statistically significantly higher opioid refills in the control group compared to the intervention group.[35] Another RCT in patients undergoing mastectomy with immediate, implant based breast reconstruction did not identify a difference between groups.[33] The two RCTs that included shared decision making around total opioid tablets prescribed found conflicting results.[36,37] One study of patients undergoing minimally invasive hysterectomy reported more refills in the patient directed arm compared to the control group.[36] The other study of patients undergoing isolated mid-urethral sling placement found no statistically significant differences in refills between groups.[37]

Three of the RCTs assessed patient satisfaction.[35-37] Only one RCT found statistically significant differences, with the intervention group being more likely to be satisfied with their pain management.[35]

Two RCTs evaluated healthcare utilization.[34,36] One RCT evaluated unexpected visits to the emergency department or to the office due to uncontrolled pain and found no differences between groups.[36] The other assessed for "serious adverse events" defined as those that led to a call or unplanned return visit to the clinic or hospital setting. There were no differences between groups.[34]

We determined the SOE to be low for the outcome of pain.

4.2.5.3.2 Opioid Prescribing or Ordering Outcomes

Five of the six RCTs evaluating patient and family education or engagement interventions assessed opioid prescribing or ordering outcomes (Table 6). All five assessed opioids prescribed after surgery, with mixed results. Three of the five had no significant differences between groups in opioids prescribed or dispensed.[33-35] The two studies comparing a shared decision-making model with standard of care did report a statistically significantly lower amount of opioids post-operatively in the intervention arm compared to the control group.[36,37]

One RCT also evaluated inpatient MME doses and found no differences between groups.[33]

We determined the SOE to be low for the outcome of opioid prescribing.

4.2.5.3.3 Changes in Process Outcomes

None of the RCTs evaluating patient and family education or engagement interventions assessed the process outcomes defined in our inclusion criteria.

Table 6. Overview of clinical outcomes and opioid prescribing/ordering outcomes for patient and family education or engagement interventions reported in the primary studies

Author, Year Study Design	Intervention Description	Opioid Prescribing Outcome at Baseline	Opioid Prescribing Outcome Post-Implementation	Pain Outcomes	Patient Satisfaction Outcomes	Healthcare Utilization Outcomes
Delara, 2022[36] RCT	A shared decision-making framework using a written script to guide the research staff to initiate conversation with the patient, describing the reason for opioid prescribing, common side effects and risks of taking opioids, and recommended management of pain. Using this framework, patients were provided the opportunity to give insight into the number of opioid tablets that they felt were appropriate for their post-operative management, which was then prescribed by the research team (up to 30 tablets)	**Number of oxycodone pills prescribed at preoperative visit, median (IQR)** Result =15 (12 - 24) (intervention) vs 30 (30 - 30) (control), p < 0.01	**Number of patients prescribed additional oxycodone after preoperative visit** Result = 5 (intervention) vs 0 (control), p=0.05	NR	**Patient satisfaction (yes vs no), n (%)** Result =29 (90.6) (intervention) vs 27 (87.1) (control), p=0.66	**Unexpected visits to the ED due to uncontrolled pain, n (%)** Result =2 (6.1) (intervention) vs 0 (0) (control), p=0.49 **Unexpected visits to the office due to uncontrolled pain, n (%)** Result=1 (3) (intervention) vs 1 (3.1) (control), p > 0.99
Voepel-Lewis, 2021[34] RCT	Routine instruction plus the Scenario-Tailored Opioid Messaging Program educational intervention, designed to provide scenario-specific opioid risk and benefit information meant to promote better decisions toward pain and ADE reduction	**Opioid doses dispensed, mean (SD)** Result = 22 +/- 16.48 (intervention) vs 21.5 +/- 13.76 (control) **Opioid doses dispensed, mean difference (95% CI)** Result = 0.5 (-1.95 to 2.96)	NR	**Child self-reported pain scores, mean (SD)** Result = Intervention vs Control Days 1 to 3; 4.9 (2) vs 4.9 (2) Days 4 to 7; 4 (2.1) vs 3.8 (1.8) Days 8 to 14; 3.5 (2.3) vs 3.2 (1.9)	NR	**Serious adverse events, n (%)** defined as events that led to a call or unplanned return visit to the clinic or hospital setting Result =9 (3.3) (intervention) vs 10 (3.4) (control)

Author, Year Study Design	Intervention Description	Opioid Prescribing Outcome at Baseline	Opioid Prescribing Outcome Post-Implementation	Pain Outcomes	Patient Satisfaction Outcomes	Healthcare Utilization Outcomes
				Parent-reported pain interference score day 14, mean (SD) Result = 8.63 (8.39) (intervention) vs 8.06 (8.06) (control)		**Serious adverse events, Odds Ratio (95% CI)** Result = 0.93 (0.37 to 2.33)
Stepan, 2021[35] RCT	Standard presurgical counseling and standardized perioperative pain management consisting of 7 minutes of education on postoperative pain management via video along with a laminated card with a summary of the preoperative pain education as part of postoperative instructions	**Pills prescribed, mean (range)** Result = 15 (5 - 50) (intervention) vs 20 (5 - 40) (control)	**Refilled prescription, n (%)** Result = 2 (2.6) (intervention) vs 9 (10.5) (control), p=0.046	**Average week-1 pain, median (range)** Result = 3.3 (0 - 9.3) (Intervention) vs 3.6 (0 - 9.1) (Control), p=0.27	**Satisfaction survey, n (%)** **Satisfied** **Neutral** **Dissatisfied** Result = Intervention vs Control, p=0.03 73 (94.8) vs 78 (91.8) 3 (3.9) vs 0 (0) 1 (1.3) vs 7 (8.2)	NR
Long, 2022[37] Prospective, randomized, open-label, noninferiority clinical trial	No preoperative prescription for opioids with the option to receive an oxycodone prescription of ten 5-mg tablets should the patient request postoperatively	NR	**Filled an opioid prescription, n (%)** Result = 8 (19%) (intervention) vs 23 (57.5%) (control), p < 0.001 **Received an opioid refill after evaluation in an ED** Result = 1 participant in each arm	**Pain scores, difference in means (95% CI)** Result = Day 0; 0.26 (- 0.72 to 1.24), p=0.6 Day 1; 0.23 (- 0.74 to 1.2), p=0.64 Day 2; 0.01 (- 0.96 to 0.98), p=0.98 Day 3; -0.00 (- 0.97 to 0.97), p=1	**Mean pain satisfaction, mean (SD)** Result = 4 (0.9) (intervention) vs 4.1 (0.8) (control), p=0.3	NR

Author, Year Study Design	Intervention Description	Opioid Prescribing Outcome at Baseline	Opioid Prescribing Outcome Post-Implementation	Pain Outcomes	Patient Satisfaction Outcomes	Healthcare Utilization Outcomes
				Day 4; -0.15 (- 1.13 to 0.82), p=0.75 Day 5; 0.46 (- 0.52 to 1.44), p=0.36 Day 6; -0.21 (- 1.19 to 0.77), p=0.67 Day 7; 0.42 (- 0.56 to 1.4), p=0.4		
Egan, 2020[33] RCT	Brief patient-based educational intervention using an educational instrument containing information about pain expectations and goals, examples of opioid and adjunct medications which may be used perioperatively, risks associated with opioid use and examples of non-medication pain control methods and statements to normalize the pain experience for the patient	**Inpatient MME, mean (SD)** Result = 27.1 (22.9) (intervention) vs 32.1 (21.1) (control) **Postop opioid prescription number, mean (SD)** Result = 35.3 (5.5) (intervention) vs 36.8 (6.7) (control)	**Opioid Refills, n (%)** Result = 6 (15%) (intervention) vs 10 (22%) (control), p=0.3 **Total opioid tablets prescribed including refills, mean (SD)** Result = 39.2 (11.9) (intervention) vs 46.6 (21.8) (control), p=0.04	**Average postop pain scores, mean (SD)** Result = 3 (1.8) (intervention) vs 3.6 (1.6) (control), p=0.06	NR	NR
Syed, 2018[32] RCT	Formal education detailing recommended postoperative opioid usage, side effects, dependence, and addiction via a 2-minute narrated video and a handout detailing the risks of	NR	NR	**Average visual analog scale pain score at followup, mean (SD)** Result = Intervention vs Control At 2 weeks; 3.3 (2.2) vs 4.4 (2.5), p=0.008	NR	NR

Author, Year Study Design	Intervention Description	Opioid Prescribing Outcome at Baseline	Opioid Prescribing Outcome Post-Implementation	Pain Outcomes	Patient Satisfaction Outcomes	Healthcare Utilization Outcomes
	narcotic overuse and abuse			At 6 weeks; 2.4 (2) vs 3.7 (2.4), p=0.001 At 3 months; 2.2 (2.4) vs 2.2 (2.2) m, p=0.2		

ADE = adverse drug effects; CI = confidence interval; ED = emergency department; EHR = electronic health record; IQR = Interquartile range; MEDD= morphine equivalent daily dose; MME = morphine milligram equivalents; OR = odds ratio; RCT = randomized controlled trial; SD = standard deviation; vs = versus

4.2.5.4 Interventions Focused on Tracking, Monitoring, and Reporting Performance Data Related to Prescribed or Ordered Opioids

Intervention categories in this section include clinical audits and dashboards.

4.2.5.4.1 Clinical Audits

One systematic review addressed patient-controlled analgesia safety monitoring in acute care and found a decreased overdose rate in one study.[21] This review found no change in opioid prescribing. The review did not grade the SOE.

4.2.5.4.2 Dashboards

No studies met our inclusion criteria for addressing dashboards alone.

4.2.5.5 Interventions Focused on Clinical Accountability Related to Prescribed or Ordered Opioids

Intervention categories in this section include prescriber feedback and peer comparison.

4.2.5.5.1 Prescriber Feedback

No studies met our inclusion criteria for addressing prescriber feedback alone.

4.2.5.5.2 Peer Comparison

One systematic review found that in interrupted time series studies there was a reduced rate of opioid prescribing with a change of -28.10 (95% CI, -44.83 to -11.38), and in a combined analysis of pre-post studies, cohort studies and RCTs there was a reduced rate of opioid prescribing, OR 0.46 (95% CI, 0.29 to 0.72).[24] The review did not grade the SOE.

We also identified one RCT that assessed an intervention focused on clinical accountability related to prescribed or ordered opioids.[38] This study randomized Veterans Health Administration (VHA) facilities to receive a notice describing a new dashboard based on the Stratification Tool for Opioid Risk Mitigation (STORM). It also described the importance of risk mitigation strategies and mandated case review. The intervention arm received the same notice with an extra paragraph stating that facilities which did not meet a target of 97 percent case reviews would receive technical assistance and be required to submit an action plan on improving the review rate. The RCT found no statistically significant difference in serious adverse events or death between groups (hazard ratio (HR) 1 (95% CI, 0.91 to 1.09) for all-cause mortality and 1.03 (95% CI, 0.97 to 1.08) for any serious adverse event). The RCT did not evaluate opioid prescribing or process outcomes.

We determined the SOE to be insufficient for the outcome of serious adverse events.

4.2.5.6 Multicomponent Interventions Focused on Opioid Stewardship

We identified one overview of systematic reviews and three additional systematic reviews that addressed multicomponent interventions.

The overview of systematic reviews [20] focused on patient-targeted interventions for opioid prescribing in any setting and included 4 reviews published from 2011 to 2021. These reviews focused on chronic pain in ambulatory settings and (a) multidisciplinary pain programs[57-59] and (b) multicomponent tapering down opioids support interventions, such as dose reduction protocols, opioid replacement, and nonpharmacologic therapies.[57,60] For opioid outcomes, multidisciplinary pain programs were consistently associated with reduced opioid prescribing compared to usual care,[57,58] with low certainty of evidence.[20] One review concluded that tapering down opioids support programs were consistently associated with reduced opioid prescribing compared to usual care.[58] The other review found that patient-focused interventions were not associated with opioid dose reduction in the intermediate term and did not increase the number of individuals able to stop opioids;[60] the certainty of evidence was low.[20] One of the systematic reviews also addressed multicomponent clinician-focused interventions consisting of training plus decision tools, and identified one study that reported a statistically significant difference in opioid dose reduction.[60]

For clinical outcomes, both types of patient-targeted interventions showed improved or unchanged pain,[57-59] with low certainty of evidence.[20]

Three additional systematic reviews addressed multicomponent interventions.[16,21,23] These interventions often included clinician education as well as system policies or guidelines on opioids and emphasized nonopioid approaches, protocols, audit and feedback, and patient involvement. System policies combined with other interventions were associated with decreased opioid prescribing. These multicomponent interventions included policy limits on number of opioid pills prescribed together with, clinician education,[16,21] discharge prescribing workflow changes,[23] and adverse event monitoring with computerized order entry or opioid safety guidelines. There were mixed results on the effect of multicomponent interventions in acute care on opioid prescribing, but an increase in nonopioid analgesic use. These multicomponent interventions included clinician education emphasizing nonopioid approaches in addition to protocols, audit and feedback or patient involvement.[21]

For clinical outcomes, system policies of number of opioid pills prescribed together with and clinician education[16] was associated with no significant difference in pain intensity. There were mixed results associated with the effects of multicomponent interventions including clinician education (emphasizing nonopioid approaches and protocols), audit and feedback, or patient involvement[21] on hospital length of stay. The multicomponent interventions were associated with reduced hospital readmissions and increased patient satisfaction with pain

treatment. Adverse event monitoring combined with computerized order entry or opioid safety guidelines[21] had no change in hospital length of stay or mortality.

Eight primary studies (reported in 9 articles) addressed multicomponent interventions (Table 7)]. We report the findings from these primary studies by outcomes below.

4.2.5.6.1 Clinical Outcomes

Four RCTs described in five articles and four nonrandomized studies assessed the effect of multicomponent interventions on clinical outcomes (Table 7). These multicomponent interventions most typically involved a combination of opioid education to prescribers, academic detailing, nurse care management and facilitated access to additional specialists. The majority of RCTs[40-42,45] were conducted on ambulatory care patients on long-term opioid therapy. One RCT was conducted with adult patients who visited an emergency department more than 10 times over a 12-month period, with at least two of those visits attributed to pain or "drug-seeking behaviors."[39] One RCT conducted in the emergency department focused on two components: a case manager and a multidisciplinary collaboration to develop individualized plans for providers to access the next time the patient presented to the emergency department.[39]

Four RCTs assessed several clinical outcomes including opioid refills, pain, patient satisfaction and healthcare utilization. Two RCTs described in 3 articles reported on opioid refill requests.[40-42] There were no differences in early refill requests between groups in either study.[40,41]

One RCT (reported in 2 articles) assessed patient satisfaction.[41,42] There were no differences between groups in high patient satisfaction (defined as a score in the top quartile) or high patient trust in provider (defined as a score in the top quartile).

Two RCTs (reported in 3 articles) reported on pain outcomes with no differences identified between groups in either study.[41,42,45] One RCT[39] conducted in emergency departments reported on healthcare utilization and found the intervention group experienced a decrease in the incidence of emergency department visits over the 12-month study period and had a lower average number of emergency department visits over the study period.

One nonrandomized study evaluated the impact of the VHA's Opioid Safety Initiative (OSI) on opioid prescribing patterns and opioid toxicity.[44] The OSI comprised five components: (1) prescribing dashboards which aggregated and reported opioid prescribing on the facility-, provider-, and patient-level; (2) clinical practice guidelines for safe prescribing; (3) provider education; (4) a complementary integrative health initiative; and (5) a stepped care model and pain management teams. A second nonrandomized study evaluated the VHA's Whole Health Primary Care Pain Education and Opioid Monitoring Program (PC-POP) for patients seen in primary care who receive long-term opioid therapy for chronic noncancer-related pain.[47] PC-POP includes components such as chart review, education, evaluation (patient self-assessments of anxiety, depression, physical

functioning, drug use/abuse, and quality of life), prescription and action (e.g., treatment planning and follow up) implemented by a multidisciplinary care team. Two nonrandomized studies evaluated opioid stewardship interventions in surgical services. One study prospectively evaluated the impact of opioid minimizing and opioid eliminating strategies in surgical patients undergoing inguinal hernia repair or cholecystectomy. Patients were grouped into one of three conditions: (1) control in which patients received standard of care with no changes, (2) opioid-sparing in which patients received patient education, perioperative multimodal analgesia, and opioid prescription at discharge, and (3) zero-opioid wherein patients received the same opioid-sparing protocol but were not provided an opioid prescription at discharge.[46] The second surgical services study reported the results of a quality improvement study evaluating the implementation of an opioid-free discharge protocol in patients undergoing ureteroscopy for urolithiasis.[43] The protocol included medication and patient counseling interventions at five stages of perioperative care: pre-operative clinic, preoperative surgical staging, intraoperative, postanesthetic care, and discharge.

Four nonrandomized studies, two conducted in the outpatient setting[44,47] and two in surgical services,[43,46] included patient reported outcomes or emergency department utilization and hospital admission outcomes. A segmented regression of pre-OSI (n = 19,382) and post-OSI (n = 22,682) opioid naïve patients treated for prostate, lung, breast or colorectal cancer at a VHA facility revealed a statistically significant increase in pain-related emergency department visits in post-intervention patients.[44] There were no significant differences between PC-POP enrollees (n = 423) and non-enrollees (n = 311) in emergency department visits or inpatient hospitalizations.[47] One study conducted in surgical services found no significant differences in patient-reported pain scores or satisfaction two weeks post-discharge.[46] The other study found no differences in emergency department visits between groups.[43]

We determined the SOE to be low for the outcome of pain.

4.2.5.6.2 Opioid Prescribing or Ordering Outcomes

Three RCTs[39,40,45] reported on opioid prescribing or ordering outcomes [Table 7]. Two RCTs found statistically significant decreases in opioid prescribing.[39,40] One RCT, targeting interventions in emergency departments, found a decrease in the odds of receiving an opioid prescription from an emergency department provider as well a smaller average number of opioid prescriptions written over 12 months in the intervention group compared to controls. Another RCT, in primary care, identified an adjusted difference in daily opioid dose of -6.8 MME ($p < 0.001$). Another third RCT, in primary care, found no difference in prescription opioid dose in MME at final visit.[45]

Three nonrandomized studies reported opioid prescribing or ordering outcomes. The study evaluating the VHA's OSI program found a statistically significant decrease in the monthly rate of new opioid prescriptions after OSI

implementation.[44] Evaluation of the PC-POP program revealed no significant differences between PC-POP enrollees and non-enrollees in suboxone doses or MME daily dose.[47] One study in surgical services found enrolled patients were less likely to have an opioid prescription at discharge as well as significantly lower morphine equivalent doses.[43]

We determined the SOE to be low for the outcome of opioid prescribing.

4.2.5.6.3 Changes in Process Outcomes

Two RCTs reported in 3 articles assessed process outcomes including urine drug testing, presence of an opioid treatment agreement, prescription drug monitoring program reports review, and achievement of guideline concordant care.[40-42] Both RCTs assessed use of urine drug screening and opioid treatment agreements. Both RCTs found that the intervention arm was more likely to undergo urine drug testing (71% versus 20%, adjusted OR 13.38 (95% CI, 5.85 to 30.6) in one study, and 74.6% versus 57.9%, $p < 0.001$ in the other study) and was more likely to have a signed treatment agreement (adjusted OR 61.5 (95% CI, 15.3 to 247.2) in one study, and 53.8% versus 6%, $p < 0.001$ in the other study) when compared to controls.

One RCT evaluated achievement of guideline concordant care (defined as urine drug testing and presence of an opioid treatment agreement) and found that the intervention group was more likely to have guideline concordant care than controls (65.9% versus 37.8%, $p < 0.001$).[40]

Another RCT assessed for use of the prescription drug monitoring program and found no statistically significant differences between groups (adjusted OR 3.85 (95% CI, 0.99 to 14.93).[41,42]

One nonrandomized study included process outcomes.[47] The study evaluating the PC-POP program found rates of naloxone prescriptions, urine drug screens, STORM reports generated, assessments for mental health, substance use, and well-being were significantly more frequent for PC-POP enrollees when compared to non-enrollees ($p < 0.001$ for all comparisons). No difference in prescription drug monitoring program reports were found between groups ($p = 0.428$). Enrollees were also more likely to be referred to nonpharmacological treatment (i.e., cognitive behavioral therapy for chronic pain, whole health, living with chronic conditions, and trauma sensitive yoga) than non-enrollees ($p < 0.001$ for all comparisons) except for mindfulness center referrals which showed no difference in between enrollees and non-enrollees ($p = 0.132$).

We did not grade the SOE for process outcomes.

Table 7. Overview of clinical outcomes and opioid prescribing/ordering outcomes for multicomponent interventions reported in the primary studies

Author, Year Study Design	Intervention Description	Opioid Prescribing Outcome at Baseline	Opioid Prescribing Outcome Post-Implementation	Pain Outcomes	Patient Satisfaction Outcomes	Healthcare Utilization Outcomes
Samet, 2021; Colasanti, 2022[41, 42] Cluster randomized control trial	Targeting Effective Analgesia in Clinics for HIV intervention consisting of: (1) a nurse care manager with an IT-enabled electronic registry to manage patients; (2) opioid education and academic detailing; and (3) facilitated access to addiction treatment specialists.	**MME, mean (SD)** Result = 28.4 (40.8) (intervention) vs 36.3 (49.3) (control),	**1 or more early refills over 12 months, %** Result = 21.6% (intervention) vs 30.4% (control), p=0.11 **1 or more early refills over 12 months, adjusted OR (95% CI)** Result = 0.55 (0.26 to 1.15), p=0.11 **No. of early refills over 12 months, mean (SD)** Result = 0.46 (1) (intervention) vs 0.6 (1.14) (control), p=0.21 **No. of early refills over 12 months, adjusted OR (95% CI)** Result = 0.64 (0.32 to 1.3), p=0.21	**Pain severity, mean (SD)** Result = 6.3 (2.87) (intervention) vs 5.76 (2.87) (control), p=0.91 **Pain severity, adjusted OR (95% CI)** Result = 0.1 (-1.56 to 1.75), p=0.91 **Pain interference, mean (SD)** Result = 5.7 (2.98) (intervention) vs 4.99 (3.58) (control), p=0.72 **Pain interference, adjusted OR (95% CI)** Result = 0.3 (-1.34 to 1.95), p=0.72	**Patient satisfaction with the way the clinic manages pain (75% percentile, range 1 - 10), n (%)** Result = 31 (54.4) (intervention) vs 27 (56.3) (control), p=0.72 **Patient satisfaction with the way the clinic manages pain (75% percentile, range 1 - 10), adjusted mean difference (95% CI)** Result = 1.17 (0.5 to 2.76), p=0.72	NR
Morasco, 2022[45] Cluster randomized control trial	Improving the Safety of Opioid Therapy intervention consisting of (1) 2-hour educational session for clinicians on patient-centered care surrounding prescription opioid adherence monitoring, (2) a nurse care manager who met with patients to provide education. The nurse care manager tailored	**Opioid dose in MED, mean (SD)** Result = 46.8 (51) (intervention) vs 37.3 (65.3) (control), p=0.167	**Prescription opioid dose in mg morphine equivalents at final visit, mean (SD)** Result = 34.4 (34.8) (intervention) vs 33.6 (42.2) (control), p=0.57	**Pain intensity score, mean (SD)** Result = Intervention vs Control Baseline; 67 (14.5) vs 65.8 (15.5) 6 months; 64.9 (16.3) vs 65.3 (17)	NR	NR

Author, Year Study Design	Intervention Description	Opioid Prescribing Outcome at Baseline	Opioid Prescribing Outcome Post-Implementation	Pain Outcomes	Patient Satisfaction Outcomes	Healthcare Utilization Outcomes
	recommendations to the PCP about improving opioid safety and (3) access for the nurse case manager to an internal medicine physician with expertise in chronic pain treatment and psychologist with expertise in treating pain and substance use disorder for recommendations as needed.			12 months; 64.9 (16.5) vs 62.1 (18) p=0.377" **Pain interference score, mean (SD)** Result = Intervention vs Control Baseline; 58.7 (28.1) vs 54 (28) 6 months; 55.6 (28.6) vs 53.3 (28.9) 12 months; 53.4 (28.7) vs 48.2 (28.9), p=0.698		
Liebschutz, 2017[40] Cluster randomized control trial	Transforming Opioid Prescribing in Primary Care intervention (nurse care management, electronic registry, academic detailing, and electronic decision tools).	**MEDD, mg n (%)** Result = Intervention vs Control, p=0.27 0;16 (2.7) vs 5 (1.3) > 0 to < 50; 392 (66.9) vs 257 (64.4) 50 – 100; 93 (15.9) vs 74 (18.6) > 100; 85 (14.5) vs 63 (15.8) **MEDD, mean (SD), mg** Result = 61.1 (84.9) (intervention) vs 62.3 (75.6) (control), p=0.84	**MEDD, mean (SD), mg** Result = 60.8 (93.7) (intervention) vs 67.3 (80.4) (control), p=0.31 **>= 2 early refills n (%)** Result = 121 (20.7) (intervention) vs 80 (20.1) (control), p=0.82	**NR**	NR	NR

Author, Year Study Design	Intervention Description	Opioid Prescribing Outcome at Baseline	Opioid Prescribing Outcome Post-Implementation	Pain Outcomes	Patient Satisfaction Outcomes	Healthcare Utilization Outcomes
		>= 2 early refills n (%) Result = 145 (24.7) (intervention) vs 94 (23.6) (control), p=0.67				
Neven, 2016[39] RCT	Information-exchange assisted citywide ED program consisting of: (1) care coordination via the ED case manager to assist with barriers to care, and (2) creation of patient specific ED Care Guidelines via a multidisciplinary committee and documented in the ED information exchange system that faxed the guideline to the provider when the patient presented to participating EDs.	**Number of opioid prescriptions from the ED in prior 12 months, mean (SD)** Result = 3.97 (3.97) (intervention) vs 3.65 (3.69) (control), p=0.61	**Opioid prescriptions from the ED, mean (SD)** Result = 0.28 (0.74) (intervention) vs 1.44 (2.05) (control), p < 0.001 **Opioid incidence in the ED (count per month), OR (95% CI)** Result = 0.208 (0.122 – 0.353), p < 0.001 **Opioid in ED (yes/no), OR (95% CI)** Result = 0.198 (0.120 – 0.325), p < 0.001	**NR**	**NR**	**ED visit incidence (count per month), OR (95% CI)** Result = 0.663 (0.569 – 0.775), p < 0.001 **ED visit (yes/no per month), incident rate ratio (95% CI)** Result = 0.673 (0.538 – 0.841), p < 0.001 **ED visits, mean (SD)** Result = 5.59 (4.65) (intervention) vs 8.49 (7.02) (control), p=0.003
Kasman, 2021[43] Prospective cohort	The opioid-free protocol at discharge involved 5 steps: (1) preoperative clinic visit, (2) preoperative surgical staging area, (3) intraoperative, (4) postanesthetic care unit, and (5) discharge.	**Opioid prescription at discharge, %** Result = 3.7% (intervention) vs 88.9% (control), p < 0.001	**Post-discharge opioid prescription, %** Result = 3.7% (intervention) vs 1.9% (control), p=0.56 **Post-discharge average MED, mean**	**NR**	NR	**Pain related phone calls, %** Result = 7.4% (intervention) vs 7.4% (control), p=1 **Pain related clinic visit, %**

Author, Year Study Design	Intervention Description	Opioid Prescribing Outcome at Baseline	Opioid Prescribing Outcome Post-Implementation	Pain Outcomes	Patient Satisfaction Outcomes	Healthcare Utilization Outcomes
		Average MED at discharge, mean Result = 12.03 (intervention) vs 110.55 (control), p < 0.001	Result = 2.11 (intervention) vs 1.85 (control), p=0.92			Result = 0% (intervention) vs 0% (control), p=1 **Pain related ED visit, %** Result = 3.7% (intervention) vs 3.7% (control), p=1
Vitzthum, 2022[44] Observational study with a comparison group	OSI: A program dashboard aggregated patient-, clinician-, and facility-level data on opioid prescribing, including high-risk prescriptions such as high daily opioid doses and concomitant benzodiazepine prescriptions. Providers were alerted to prescribing patterns identified as high risk or deviated from the institutional standard of care.	**Median rate of new opioid prescriptions, % (IQR)** Result = 24.1 (18.7 - 36.6) (pre OSI) **Monthly rate of change of high-dose opioid prescriptions, % (95% CI)** Result = 0.4 (-0.7 - 1.5), p=0.49	**Monthly rate of change for new opioid prescriptions per month, % (95% CI)** Result = -0.3 % (-0.4 to -0.1) **Median change in prescription rates between 2016 and 2014, % (IQR)** Result = - 3.5 (-12.6 – 6) **Monthly rate of change of high-dose opioid prescriptions, % (95% CI)** Result = -0.8 (-2.2 - 1.3), p=0.26	**NR**	NR	**Pain related ED visits, incidence (95% CI)** Result = 1.8 (0.9 - 2.7) (post - OSI) vs 0.8 (0.4 - 1) (Q1 pre-OSI) or 0.3 (0.1 - 0.6) (Q3 pre-OSI) **Pain related ED visit monthly rate of change, % (95% CI)** Result = 3 (1 - 5), p=0.03 **3-year cumulative incidence of opioid related admissions** Result = 0.5 (1.1 - 1.4) (post - OSI) vs 0.9 (0.7 - 1) (pre - OSI), p < 0.001
Lamm, 2022[46]	Opioid reduction intervention protocol included: (a) an educational component at the	**Total intraoperative MME, median (IQR)**	**Total MME after discharge, median (IQR)**	**Pain scores after discharge, median (IQR)**	**Satisfaction scores after discharge, median (IQR)**	**Calls to surgeon's office with pain**

Author, Year Study Design	Intervention Description	Opioid Prescribing Outcome at Baseline	Opioid Prescribing Outcome Post-Implementation	Pain Outcomes	Patient Satisfaction Outcomes	Healthcare Utilization Outcomes
Prospective cohort	outpatient visit with the surgeon tailored to the specific procedure, as well as the American College of Surgeons Safe and Effective Pain Control After Surgery patient tool; (b) preoperative multimodal analgesia provided 1 hour prior to operation; (c) goal-directed fluid management, limited intraoperative opioid administration at the discretion of the anesthesiologist, and local anesthetic administered at incision sites; (d) limited post-anesthesia care unit administration of opioids based on pain scores (opioids only allowed for pain visual analog score > 6), discharge counseling regarding limited opioid use at home, and instructions to alternate between acetaminophen and ibuprofen every 3 hours for pain.	Result = 480 (240 - 480) (zero-opioid) vs 420 (240 - 480) (opioid sparing) vs 480 (480 - 720) (control), p=0.0001 **Total MME in PACU, median (IQR)** Result = 15 (7.5 - 15) (zero-opioid) vs 7.5 (7.5 - 15) (opioid sparing) vs 15 (7.5 - 22.5) (control), p=0.3368	Result = 0 (0) (zero-opioid) vs 15 (11 - 22.5) (opioid sparing) vs 46 (37.5-75) (control), p = 0.0001 **Pain medication refills within 30 days, n (%)** Result = 0 (0) (zero opioid) vs 4 (9.5) (opioid sparing) vs 3 (5.2) (control), p=0.218	4 (3 - 5) (zero opioid) vs 2 (1 - 3) (opioid sparing) vs 3 (1 - 4) (control), p=0.08	Result = 10 (8.5 - 10) (zero opioid) vs 10 (9 - 10) (opioid sparing) vs 10 (9 - 10) (control), p=0.8302	**within 30 days, n (%)** Result = 0 (0) (zero opioid) vs 10 (23.8) (opioid sparing) vs 10 (17.2) (control), p=0.022
Martinson, 2023[47] Observational study with a comparison group	Primary Care Pain Education and Opioid Monitoring Program is made up of an interdisciplinary care management consult team that implements the Veteran Affairs/Department of Defense guidelines for long-	NR	**MEDD dose, mean (SD)** Result = 40.96 (63.95) (intervention) vs 35.44 (58.68) (control), p=0.284	**NR**	NR	**ED visits, mean (SD)** Result = 1.09 (2.094) (intervention) vs 0.916 (1.949) (control), p=0.085

Author, Year Study Design	Intervention Description	Opioid Prescribing Outcome at Baseline	Opioid Prescribing Outcome Post-Implementation	Pain Outcomes	Patient Satisfaction Outcomes	Healthcare Utilization Outcomes
	term opioid therapy among patients with chronic pain in primary care.					**Inpatient hospitalizations, mean (SD)** Result = 0.289 (0.805) (intervention) vs 0.334 (0.845) (control), p=0.461

CI = confidence interval; ED = emergency department; EHR = electronic health record; HIV = human immunodeficiency virus; IQR = interquartile range; MEDD = morphine equivalent daily dose; MME = morphine milligram equivalents; NR = not reported; OSI = Opioid Sparing Initiative; OR = odds ratio; PACU= post-anesthesia care unit; RCT = randomized controlled trial; SD = standard deviation; vs = versus

4.2.5.7 Systematic Reviews Crossing Different Types of Interventions

We identified three systematic reviews that combined different intervention types: one in urologic surgery[15];one for frequent emergency department visits due to pain[25]; and part of another systematic review in the ED.[24] The interventions (which included hospital or departmental guidelines for opioid prescriptions, analgesic escalation protocols, change in default electronic medical record opioid prescription prescriber instructions, patient education and multicomponent interventions) showed a statistically significant reduction in opioid prescriptions or mean prescribed opioids on discharge,[15,24,25] with no significant worsening of patient-reported satisfaction with analgesia, number of phone calls for inadequate analgesia, or number of patients requiring emergency visits for pain.[15,24]

4.2.6 Question 6. What Are Common Barriers and Facilitators to Implementing Opioid Stewardship Practices?

One systematic review focusing on pharmacists' role in chronic noncancer pain[18] addressing barriers and facilitators. Barriers included lack of training and confidence, high volume of workload, gaps in communication, inadequate monitoring, patient reluctance and expectations, lack of a comprehensive approach, inadequate access to alternative treatments, lack of policies and protocols, and lack of clear roles. Physician and patient acceptance of the aspects of the intervention (e.g., high rates of participation in the intervention and perceived acceptance of pharmacists' role in opioid education and safety) were facilitators.

The primary effectiveness studies did not formally evaluate barriers and facilitators, although many interventions included components that could be considered facilitators. Studies about discharge prescribing often included clinician education, many studies included patient education, and studies tapering down on long-term opioids often included multidisciplinary pain management resources. We identified one excluded study that evaluated barriers and facilitators. One RCT evaluating implementation of clinical guidelines for opioid prescribing did not report clinical outcomes[61] but noted that facilitators of guideline adoption included using a personal touch for clinic engagement; clear and frequent communication; clear expectations for clinic staff; explicit instructions for implementation tools; flexibility with clinic constraints and preferences; and familiarity with organizational context, workflows, policies, and values.

4.2.7 Question 7. What Resources (e.g., Cost, Staff, Time) Are Required for Implementation of Opioid Stewardship Practices?

Systematic reviews did not report on cost, staffing, or time. Studies tapering down patients on chronic opioids often included or referred to additional resources for pain management such as case managers, cognitive behavioral therapy, or physical therapy. Cost and time were not documented in the studies that we included for effectiveness, but we did identify some additional studies that quantified this aspect of implementation. One RCT of implementing clinical guidelines for opioid prescribing (which was excluded from our review on Question 5 because it did not report clinical outcomes) reported on cost, staffing, and time.[61] Across all 4 sites, the facilitator spent 237.7 hours delivering the implementation strategy, two physician consultants combined spent 85.7 hours working with sites, and each clinic staff member spent approximately 9 hours. The total cost of delivering the intervention of the change team (not including clinic staff members' time) was $29,379 or $7345 per clinic.

4.2.8 Question 8. What Toolkits Are Available To Support Implementation of Opioid Stewardship Practices?

No toolkits were identified in the included reviews, but one primary study included a publicly available toolkit to support implementation. A toolkit is available from the U.S. VHA for the OSI program evaluated in Vitzthum, et al.[44,62] This toolkit includes educational resources for patients and clinicians, clinical practice guidelines, and resources for nonpharmacological pain management alternatives (e.g., cognitive behavioral therapy). Additionally, we identified publicly available patient safety toolkits developed by the Agency for Healthcare Research and Quality (AHRQ) and other organizations that could help support implementation of PSPs.[63]

- AHRQ's Six Building Blocks: A Team-Based Approach to Improving Opioid Management in Primary Care which focuses on improving the quality of care for patients with chronic pain who are using long-term opioid therapy.[64]
- AHRQ's Clinical Decisions Support (CDS) Connect Artifacts on Opioids and Pain Management which provides overall guidance and an implementation guide on factors to consider in managing chronic pain.[65]
- American Society of Consultant Pharmacists (ASCP) Opioid Stewardship Toolkit: A Pharmacist's Guide for Older Adults.[66]
- American Hospital Association's Stem the Tide: Addressing the Opioid Epidemic which includes a wide range of resources for clinician, patient, and community engagement and education as well as a separate measurement toolkit.[67]
- The CDC's Creating a Culture of Safety for Opioid Prescribing: A Handbook for Healthcare Executives.[68]

- Electronic Health Record Association's CDC Opioid Guideline Implementation Guide for Electronic Health Records designed to support organization's use of electronic health record-based CDS tools.[69]
- The College of Healthcare Information Management Executives' (CHIME) Opioid Taskforce Playbook which provides a framework to build information technology-based supports for Opioid stewardship initiatives.[70]
- The Society for Hospital Medicine's Reducing Adverse Drug Events Related to Opioids Implementation Guide which provides step-by-step guidance to hospital teams implementing quality improvement programs to reduce opioid-related adverse events.[71]
- The Institute for Healthcare Improvement's guide for Advancing the Safety of Acute Pain Management which provides stepwise guidance for building a safe and effective acute pain management strategy.[72]
- The Society for Hospital Medicine's Implementation Guide for Improving Pain Management for Hospitalized Medical Patients which provides a process for structuring and executing efforts to implement best practices in pain management.[73]
- Health Innovation East opioid deprescribing toolkit.[74]

5. Discussion

5.1 Summary and Interpretation of Findings

Research on opioid stewardship interventions has expanded significantly in recent years. Included systematic reviews primarily summarized pre-post studies of a wide variety of interventions including patient and family engagement, healthcare organization policy, and clinician education and training. These interventions were evaluated in various healthcare delivery settings including inpatient, perioperative, emergency department, and ambulatory care. Randomized controlled trials (RCTs) mainly addressed multicomponent interventions, most commonly prescriber education, care management and facilitated access to additional resources, and patient education and engagement, mainly studying chronic pain in the ambulatory setting.

Given the heterogeneous intervention types, delivery settings, and outcomes evaluated, we conclude that opioid stewardship patient safety practices evaluated since the release of the 2016 Centers for Disease Control and Prevention (CDC) opioid guidelines were associated with decreases in opioid prescribing or doses (low strength of evidence). With reduced opioid doses, studies did not find increases in unintended consequences of increased pain, or an increase in hospitalizations or emergency department visits (low strength of evidence). Insufficient evidence was available on opioid refills or requests, patient satisfaction or overdose.

Barriers included lack of training, workload, gaps in communication, and inadequate access to nonpharmacological resources. Clinician and patient acceptance were identified as important facilitators. We also noted an emphasis on the important role of patient engagement and education in these interventions, including in nonpharmacological approaches to pain management.

Below we summarize, by intervention category, the broader literature reported in systematic reviews (which generally did not include grading of the strength of evidence) and the high-quality primary studies (Table 8).

No reviews or primary studies were found for dashboards, prescriber feedback, or opioid stewardship committees as standalone interventions.

Table 8. Summary of the evidence by interventions

Intervention Category	Evidence Summary
Clinical decision support or electronic health record interventions	• Five systematic reviews found that CDS/EHR interventions may decrease opioid prescribing with no effect on opioid refill requests.[16,21,23,24,26] • Two RCTs found no significant difference in healthcare utilization (e.g., emergency department visits, outpatient visits, and hospitalizations) between CDS/EHR interventions and no intervention. Both RCTs found the reduced default group had significantly less opioids prescribed at baseline although one of the RCTs found an increase in opioid reordering for the reduced default group.[29,30] • One nonrandomized study found decreased emergency department opioid and barbiturate prescriptions, no change in pain scores, and mixed findings for utilization (i.e., consults, imaging, admissions) after implementation of an EHR algorithm.[28] • The strength of evidence was low for healthcare utilization and opioid prescribing.
Protocol or care bundle interventions	• One systematic review found that a protocol for using inpatient opioid consumption to guide discharge prescribing was associated with a decrease in discharge opioid prescribing.[23] • No reviews or primary studies addressed care bundle interventions in isolation. • The strength of evidence was insufficient.

Clinician education or academic detailing interventions	• Four systematic reviews addressed the interventions alone.[16,17,22,23]
	• Three of the four reviews reported the following:
	  ○ Reduced opioid prescribing after the intervention.
	  ○ Increased refill requests or pain-related complaints.
	  ○ No increase in utilization (return visits to the emergency department).

Clinical pharmacist consultation intervention	• Two included systematic reviews found a reduction in opioid dose after pharmacist intervention.[18,26]
	• Review findings for clinical outcomes were mixed:
	  ○ One review found that 5 of 8 studies showed significant reduction in pain intensity.
	  ○ The other review found no increase in post-operative pain, and no increases in utilization (hospital visits).

Increased access or emphasis on nonopioid or multimodal analgesia, and/or limits on opioid prescribing/ordering intervention	Three systematic reviews found[14,16,26]: • Opioid replacement (replacing one opioid with another) showed no significant difference in opioid dosing. • Deprescription methods in ambulatory chronic pain (with or without non-pharmacological pain management techniques), coordinated recommendations for opioid prescribing, and increasing opioid-free prescribing all reduced opioid dose or prescribing. • One review on increasing opioid-free prescribing found no differences in pain, requirement for additional prescriptions, or satisfaction.

Healthcare organization guidelines for opioids and/or emphasizing nonopioid pain medications	Three systematic reviews reported[22,23,26]:
	Decreases in prescription size and doses
	  ○ General improvement in pain
	  ○ No difference in patient satisfaction or phone calls for pain
	  ○ Mixed results for refills or requests
	• One additional primary study demonstrated reduced opioids prescribed with no change in patient satisfaction.[31]
	• The strength of evidence was insufficient.

Intervention Category	Evidence Summary
Patient and family education or engagement interventions	**Systematic reviews** • Generally found significantly reduced or discontinued opioid prescribing. • All five systematic reviews assessing pain outcomes found reductions in pain intensity.[14,16,19,22,26] • The review that assessed opioid refill requests found no difference.[27] **RCTs** • Four of the five RCTs assessing pain found no statistically significant differences in pain between groups.[33-35,37] • Four RCTs reported opioid refill data, with mixed results.[33,35-37] • Three RCTs assessed patient satisfaction.[35-37] • One RCT reported statistically significant differences, with the intervention group being more likely to be satisfied with their pain management.[35] The other two RCTs reported no significant differences between conditions. • Two RCTs evaluated healthcare utilization and found no differences. [34,36] • Five RCTs assessed opioid prescribing or ordering outcomes after surgery with three trials showing no significant differences and two trials reporting a statistically significant reduced amount of opioids* in the intervention arm compared to the control group. .[33-37] One RCT evaluated inpatient opioid doses and found no differences between groups.[33] • The strength of evidence was low for pain and low for opioid prescribing.
Clinical audit interventions	• A systematic review found a decreased overdose rate in one study.[21] • The review also found no change in opioid prescribing.
Peer comparison interventions	• A systematic review found reduced opioid prescribing.[24] • One RCT of a clinical accountability intervention found no statistically significant difference in serious adverse events or death between groups but did not evaluate opioid prescribing or process outcomes.[38] • The strength of evidence for peer comparison interventions is insufficient.
Multicomponent interventions	Two types of interventions addressed: **In Hospital settings:** System policies on opioid prescribing, workflow changes, dashboards, prescriber or patient education. **In Ambulatory settings:** Prescriber education with case management and improved access to alternative resources in patients with chronic pain while providing patient education and/or nonpharmacological pain management support. • Systematic reviews concluded that both intervention types were generally associated with reduced opioid prescribing with unchanged or improved pain. [16,21,23,20] • Additional primary studies generally saw no increase in unintended consequences of pain, early refills or requests, dissatisfaction, and emergency department visits or hospitalizations in the intervention group compared to the control group.[39-47] • Additional primary studies generally found associations with reduced opioid prescribing in the intervention group compared to the control group (5 studies found a reduction and 2 studies found no difference). • The strength of evidence was low for pain and low for opioid prescribing.

CDS =Clinical decision support; EHR= electronic health record; RCT =Randomized controlled trials

*"Amount of opioids" when used in these studies means "number or amount of pills"

5.2 Limitations

We note limitations both of this rapid review and of the literature. Since peaking in 2012, opioid prescribing in the United States has markedly decreased over recent years. This trend might be influenced by a variety of factors including increased recognition of the negative societal impacts of opioid overprescribing, the CDC and other prescribing guidelines, state and federal education, legislative initiatives, and prescribing norms. Thus, it is challenging to interpret the specific impact of interventions evaluated in pre-post studies. We therefore focused on studies with stronger designs, but because these mainly focused on only a few types of interventions, we also descriptively summarized systematic reviews which included pre-post studies to acknowledge the broader lower quality evidence for other kinds of interventions.

We limited our review to systematic reviews and studies that addressed clinical outcomes. Although this ensured that we evaluated the potential patient-centered unintended consequences of reduced opioid prescribing, this excluded some studies of interventions in settings such as the emergency department where followup information on pain outcomes may be limited. However, we included systematic reviews and studies in the emergency department. The studies also included evaluations of unintended consequences of changes in pain, opioid refills, hospitalizations, and emergency department use outcomes for which we found low strength of evidence.

The systematic reviews had important limitations. In particular, systematic reviews generally did not synthesize the literature but summarized the results of individual studies. We also found significant overlap between the studies addressed in the systematic reviews. In addition, some of the reviews included studies that were out of the scope of our review (e.g., studies outside the United States). Because of challenges with the quality of the systematic review methods and their heavy dependence on pre-post studies and lack of evidence grading, we reviewed RCTs and nonrandomized studies dating back to 2016 (the release of the CDC opioid prescribing guidelines) and used these studies as our primary source for drawing conclusions and grading the strength of evidence.

We rated all nonrandomized studies, and all but one of the RCTs, as having a high risk of bias, usually due to lack of blinding for outcome assessments, among other issues. Some earlier systematic reviews often rated the risk of bias of pre-post studies and some of the RCTs as moderate or low risk of bias. We reviewed all RCTs dating back to 2016 and based our grading only on the primary studies. Some of the earlier systematic reviews rated the strength of evidence as low for opioid prescribing outcomes, but other reviews, including Making Healthcare Safer III, rated the strength of evidence for opioid prescribing as moderate. Prior reviews did not consistently provide their methods for assessing risk of bias and strength of evidence, so we noted when our assessments differed from the prior assessments.

We included a summary of our assessments of the risk of bias of included primary studies since 2016 (see Figures 3 and 4).

5.3 Implications for Clinical Practice and Future Research

5.3.1 Implication for Clinical Practice

The increased scope and quality of evaluations of opioid stewardship interventions since 2016 can help guide the implementation of guidelines into clinical practice. A number of studies focused on tapering down opioids for chronic pain in the ambulatory setting, often in conjunction with multidisciplinary pain management and nonpharmacologic approaches to reduce opioid use. The studies demonstrated that opioids can be tapered and used in lower doses with similar or improved pain outcomes if additional resources are provided. Another large category of studies included EHR and decision support initiatives such as decreasing the default opioid prescription, generally without worsening unintended consequences. Another focus was on health system prescribing guidelines on appropriate indications for opioids after certain procedures.

Most studies addressing unintended consequences did not find worsened pain when fewer or lower doses of opioids were prescribed. However, these studies did not often assess requests for refills as a potential unintended consequence and they often did not use rigorous methods for pain measurement and detailed followup. Patient reported outcomes were also generally evaluated in a limited way when included, with a focus on pain intensity and sometimes patient satisfaction, but less often important domains such as functional status. Studies were generally small and underpowered to evaluate requests for refills, emergency room visits, hospitalizations, or other consequences of uncontrolled pain. Studies were also underpowered to evaluate the effect of these interventions on reducing overdoses, a relatively rare adverse consequence of opioid ordering and prescribing in the short term but a very important issue with chronic use, as are self-harm and suicide attempts; these should be addressed in future long-term followup research.

5.3.2 Future Research

In 2022, the CDC updated the clinical practice guideline[3] with the stated justification to address unintended consequences of misapplication of the 2016 guideline, specifically inadequate treatment for pain or abrupt discontinuation of opioids and stigma for the treatment of chronic pain and prescription opioid use. The findings of this review support that approaches such as including alternative modalities for pain control with opioid stewardship patient safety practices might help prevent unintended adverse consequences such as increased pain. Opioids play a critical role in some acute pain and chronic pain management situations, so

flexibility and patient-centered care remains essential to meet the needs of individual patients.

Future research also needs to incorporate the effects of interventions on disparities in pain management, ensuring they do not exacerbate known disparities in appropriate opioid prescribing. Future research on increasing access to nonpharmacologic pain management resources is needed on how best to improve opioid stewardship, without worsening pain outcomes. Interventions in practice should ideally include meaningful education and engagement of patients on the role of opioids and management and provide alternative pain resources. Unintended consequences need to be monitored and programs should ensure that access and support persists so that issues with uncontrolled pain can be addressed. New research is needed on commonly used interventions such as opioid stewardship committees, dashboards and peer comparisons, and care bundle interventions such as urine drug testing, treatment agreements and prescription drug monitoring program queries. These interventions require staff time and effort, and older evidence supporting them might be less relevant with reduced opioid prescribing patterns and increased health information exchange use. We may need more research to evaluate their effectiveness and costs in the current landscape.

Many of these types of interventions were addressed only in pre-post studies. System-level interventions are not as amenable to RCT approaches. To improve the quality of research, future studies, when applicable, should include blinding of outcome assessments.

The impact of factors outside health facilities and systems, such as health insurance prior authorization for opioids and lack of coverage for non-pharmacological interventions, was outside the scope of our review but can impact prescribing. Future research on the impact of factors outside of the healthcare delivery setting is needed. Future reviews should also address the outcome of examination of unused opioids from prescriptions in the setting of acute pain management. We also note that lack of access to or long wait times for nonpharmacological pain management resources present challenges to patient care. Future research on the social determinants of health may also provide insight on ways to improve pain management and opioid safety.

6. References

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Afterword

Recognized for excellence in conducting comprehensive systematic reviews, the Agency for Healthcare Research and Quality (AHRQ) Evidence-based Practice Center (EPC) Program is developing a range of rapid evidence products to assist end-users in making specific decisions in a limited timeframe. AHRQ recognizes that people are struggling with urgent questions on how to make healthcare safer. AHRQ is using this rapid format for the fourth edition of its Making Healthcare Safer series of reports, produced by the EPC Program and the General Patient Safety Program. To shorten timelines, reviewers make strategic choices about which processes to abridge. However, the adaptations made for expediency may limit the certainty and generalizability of the findings from the review, particularly in areas with a large literature base. Transparent reporting of the methods used and the resulting limitations of the evidence synthesis are extremely important.

AHRQ expects that these rapid evidence products will be helpful to health plans, providers, purchasers, government programs, and the healthcare system as a whole. Transparency and stakeholder input are essential to AHRQ. If you have comments related to this report, they may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 5600 Fishers Lane, Rockville, MD 20857, or by email to MHS@ahrq.hhs.gov.

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Appendixes

Appendix A. Methods

Search Strategies for Published Literature

Table A-1. PubMed search strategy

#	Concept	Search Terms
1	Opioid	"Analgesics, Opioid"[Mesh] OR opioid [tiab] OR opioids [tiab] OR opiate [tiab] OR opiates [tiab] OR "morphine milligram equivalents" [tiab]
2	Intervention	“Decision Support Systems, Clinical” [mh] OR “Health Information Exchange” [mh] OR “Health Information Systems” [mh] OR “Prescription Drug Monitoring Programs” [mh] OR “Drug Monitoring” [mh] OR “Stewardship” [tiab] OR “Prescription Drug Monitoring Program” [tiab] OR “Treatment Agreement” [tiab] OR “Patient Contract” [tiab] OR “risk assessment” [tiab] OR “Clinical Decision*” [tiab] OR “Health Information Technology” [tiab] OR “Monitoring” [tiab] OR “Patient Registry” [tiab] OR “Dashboard” [tiab] OR “Feedback Approach” [tiab] OR “prescriber feedback” [tiab] OR “Electronic Health Records” [MH] OR “electronic health record” [tiab] OR intervention*[tiab] OR guideline*[tiab] OR stewardship*[tiab] OR monitor*[tiab] OR program*[tiab] OR alert*[tiab] OR benchmark*[tiab] OR protocols [tiab] OR “care bundle”[tiab] OR “clinical audit”[tiab] OR “pharmacist consultation”[tiab] OR “peer comparison” [tiab] OR restriction [tiab] OR reminder [tiab] OR “risk reduction” [tiab]
3	Patient safety/harm	"patient safety"[mh] OR "patient safety" [tiab] OR "Patient Harm"[mh] OR "Patient Harm*"[tiab] OR "patient risk*"[tiab] OR "quality care" [tiab] OR “adverse event*"[tiab] OR "undesired event*"[tiab] OR "medical errors"[mh] OR "medical error*"[tiab] OR "Diagnostic Errors" [mh] OR "diagnostic error*"[tiab] OR "diagnostic mistake*"[tiab] OR "health care error*"[tiab] OR "healthcare error*"[tiab] OR "medical fault*"[tiab] OR "medical mistake*"[tiab] OR "erroneous diagnos*"[tiab] OR "failure to diagnose"[tiab] OR "false diagnos*"[tiab] OR "faulty diagnos*"[tiab] OR misdiagnos*[tiab] OR "mistaken diagnos*"[tiab] OR "wrong diagnos*"[tiab] OR "Practice Patterns, Physicians” [Mesh] OR prescription [tiab] OR prescriptions [tiab] OR prescribing [tiab] OR “drug prescriptions” [majr] OR “drug monitoring” [majr]
4	#1 AND #2 AND #3	#1 AND #2 AND #3
5	#4 NOT	address[pt] OR "autobiography"[pt] OR "bibliography"[pt] OR "biography"[pt] OR congress[pt] OR "dictionary"[pt] OR "directory"[pt] OR "festschrift"[pt] OR "historical article"[pt] OR lecture[pt] OR "legal case"[pt] OR "legislation"[pt] OR "periodical index"[pt] OR Comment[pt] OR Letter[pt] OR Editorial[pt] OR “news”[pt] OR “newspaper article”[pt] OR “patient education handout”[pt] OR “periodical index”[pt] OR “study guide”[pt] OR rats[tw] OR cow[tw] OR cows[tw] OR chicken[tw] OR chickens[tw] OR horse[tw] OR horses[tw] OR mice[tw] OR mouse[tw] OR bovine[tw] OR sheep[tw] OR ovine OR murine[tw] OR "Case Reports"[pt] OR “cocaine use”[ti] OR “opioid use disorders”[ti] OR “opioid use disorder”[ti] OR "nursing home"[ti] OR "opioid abuse"[ti] OR "insurance"[ti] OR federal [ti] OR "opioid addiction"[ti] OR "Medication assisted treatment"[ti] OR "scoping review"[ti] OR "integrative review"[ti] OR "rapid review"[ti] OR "living review"[ti] OR "environmental scan"[ti]
6	PubMed Filter - English	
7	#6 AND 2016-April 2023	
8	#6 and PubMed Filter- “Systematic Review”	For systematic reviews only
9	#8 AND 2019 -April 2023	For systematic reviews only

Table A-2. Cochrane search strategy

#	Concept	Search Terms
1	Opioid	((opioid OR opioids OR opiate OR opiates OR "morphine milligram equivalents"):ti OR (opioid OR opioids OR opiate OR opiates OR "morphine milligram equivalents"):ab OR "Analgesics, Opioid"[Mesh]) AND ((“Stewardship” OR “Prescription Drug Monitoring Program” OR “Treatment Agreement” OR “Patient Contract” OR “risk assessment” OR “Clinical Decision*” OR “Health Information Technology” OR “Monitoring” OR “Patient Registry” OR “Dashboard” OR “Feedback Approach” OR “prescriber feedback” OR “electronic health record” OR intervention* OR guideline* OR stewardship* OR monitor* OR program* OR alert* OR benchmark* OR protocols OR “care bundle” OR “clinical audit” OR “pharmacist consultation” OR “peer comparison” OR restriction OR reminder OR “risk reduction”):ti OR (“Stewardship” OR “Prescription Drug Monitoring Program” OR “Treatment Agreement” OR “Patient Contract” OR “risk assessment” OR “Clinical Decision*” OR “Health Information Technology” OR “Monitoring” OR “Patient Registry” OR “Dashboard” OR “Feedback Approach” OR “prescriber feedback” OR “electronic health record” OR intervention* OR guideline* OR stewardship* OR monitor* OR program* OR alert* OR benchmark* OR protocols OR “care bundle” OR “clinical audit” OR “pharmacist consultation” OR “peer comparison” OR restriction OR reminder OR “risk reduction”):ab OR Electronic Health Records”[Mesh] OR “Decision Support Systems, Clinical”[Mesh] OR “Health Information Exchange”[Mesh] OR “Health Information Systems”[Mesh] OR “Prescription Drug Monitoring Programs”[Mesh] OR “Drug Monitoring”[Mesh])
2	Patient safety/harm	("patient safety" OR "Patient Harm*" OR "patient risk*" OR "quality care" OR “adverse event*" OR "undesired event*" OR "medical error*" OR "diagnostic error*" OR "diagnostic mistake*" OR "health care error*" OR "healthcare error*" OR "medical fault*" OR "medical mistake*" OR "erroneous diagnos*" OR "failure to diagnose" OR "false diagnos*" OR "faulty diagnos*" OR misdiagnos* OR "mistaken diagnos*" OR "wrong diagnos*" OR prescription OR prescriptions OR prescribing):ti OR ("patient safety" OR "Patient Harm*" OR "patient risk*" OR "quality care" OR “adverse event*" OR "undesired event*" OR "medical error*" OR "diagnostic error*" OR "diagnostic mistake*" OR "health care error*" OR "healthcare error*" OR "medical fault*" OR "medical mistake*" OR "erroneous diagnos*" OR "failure to diagnose" OR "false diagnos*" OR "faulty diagnos*" OR misdiagnos* OR "mistaken diagnos*" OR "wrong diagnos*" OR prescription OR prescriptions OR prescribing):ab OR ("Patient Harm"[Mesh] OR "patient safety"[Mesh] OR "medical errors"[Mesh] OR "Diagnostic Errors" [Mesh] OR "Practice Patterns, Physicians” [Mesh] OR “drug monitoring”[Mesh])

#	Concept	Search Terms
3	#1 AND #2	(((opioid OR opioids OR opiate OR opiates OR "morphine milligram equivalents"):ti OR (opioid OR opioids OR opiate OR opiates OR "morphine milligram equivalents"):ab OR "Analgesics, Opioid"[Mesh]) AND ((“Stewardship” OR “Prescription Drug Monitoring Program” OR “Treatment Agreement” OR “Patient Contract” OR “risk assessment” OR “Clinical Decision*” OR “Health Information Technology” OR “Monitoring” OR “Patient Registry” OR “Dashboard” OR “Feedback Approach” OR “prescriber feedback” OR “electronic health record” OR intervention* OR guideline* OR stewardship* OR monitor* OR program* OR alert* OR benchmark* OR protocols OR “care bundle” OR “clinical audit” OR “pharmacist consultation” OR “peer comparison” OR restriction OR reminder OR “risk reduction”):ti OR (“Stewardship” OR “Prescription Drug Monitoring Program” OR “Treatment Agreement” OR “Patient Contract” OR “risk assessment” OR “Clinical Decision*” OR “Health Information Technology” OR “Monitoring” OR “Patient Registry” OR “Dashboard” OR “Feedback Approach” OR “prescriber feedback” OR “electronic health record” OR intervention* OR guideline* OR stewardship* OR monitor* OR program* OR alert* OR benchmark* OR protocols OR “care bundle” OR “clinical audit” OR “pharmacist consultation” OR “peer comparison” OR restriction OR reminder OR “risk reduction”):ab OR Electronic Health Records”[Mesh] OR “Decision Support Systems, Clinical”[Mesh] OR “Health Information Exchange”[Mesh] OR “Health Information Systems”[Mesh] OR “Prescription Drug Monitoring Programs”[Mesh] OR “Drug Monitoring”[Mesh])) AND (("patient safety" OR "Patient Harm*" OR "patient risk*" OR "quality care" OR “adverse event*" OR "undesired event*" OR "medical error*" OR "diagnostic error*" OR "diagnostic mistake*" OR "health care error*" OR "healthcare error*" OR "medical fault*" OR "medical mistake*" OR "erroneous diagnos*" OR "failure to diagnose" OR "false diagnos*" OR "faulty diagnos*" OR misdiagnos* OR "mistaken diagnos*" OR "wrong diagnos*" OR prescription OR prescriptions OR prescribing):ti OR ("patient safety" OR "Patient Harm*" OR "patient risk*" OR "quality care" OR “adverse event*" OR "undesired event*" OR "medical error*" OR "diagnostic error*" OR "diagnostic mistake*" OR "health care error*" OR "healthcare error*" OR "medical fault*" OR "medical mistake*" OR "erroneous diagnos*" OR "failure to diagnose" OR "false diagnos*" OR "faulty diagnos*" OR misdiagnos* OR "mistaken diagnos*" OR "wrong diagnos*" OR prescription OR prescriptions OR prescribing):ab OR ("Patient Harm"[Mesh] OR "patient safety"[Mesh] OR "medical errors"[Mesh] OR "Diagnostic Errors" [Mesh] OR "Practice Patterns, Physicians” [Mesh] OR “drug monitoring”[Mesh]))
4.	#3 NOT	((address OR "autobiography" OR "bibliography" OR "biography" OR congress OR "dictionary" OR "directory" OR "festschrift" OR "historical article" OR lecture OR "legal case" OR "legislation" OR "periodical index" OR Comment OR Letter OR Editorial OR “news” OR “newspaper article” OR “patient education handout” OR “periodical index” OR “study guide” OR "Case Reports"):pt OR (rats OR cow OR cows OR chicken OR chickens OR horse OR horses OR mice OR mouse OR bovine OR sheep OR ovine OR murine):kw OR (“cocaine use” OR “opioid use disorders” OR “opioid use disorder” OR "nursing home" OR "opioid abuse" OR "insurance" OR federal OR "opioid addiction" OR "Medication assisted treatment" OR "scoping review" OR "integrative review" OR "rapid review" OR "living review" OR "environmental scan"):ti
5	#4 English only	
6	#5 and 2019 to April 2023 for systematic reviews	
#7	#5 and 2016 to April 2023 for non-systematic reviews	

Appendix B. List of Excluded Studies Upon Full-Text Review

Acharya PP, Fram BR, Adalbert JR, et al. Impact of an Educational Intervention on the Opioid Knowledge and Prescribing Behaviors of Resident Physicians. Cureus. 2022 Mar;14(3):e23508. doi: 10.7759/cureus.23508. PMID: 35494931. **- Qualitative study without any quantitative data**

Acquisto NM, Schult RF, Sarnoski-Roberts S, et al. Effect of pharmacist-led task force to reduce opioid prescribing in the emergency department. Am J Health Syst Pharm. 2019 Oct 30;76(22):1853-61. doi: 10.1093/ajhp/zxz204. PMID: 31557284. - **Other: Study included in previous systematic reviews**

Adalbert JR, Ilyas AM. Implementing Prescribing Guidelines for Upper Extremity Orthopedic Procedures: A Prospective Analysis of Postoperative Opioid Consumption and Satisfaction. Hand (N Y). 2021 Jul;16(4):491-7. doi: 10.1177/1558944719867122. PMID: 31441326. **- No comparison group**

Agarwal AK, Lee D, Ali Z, et al. Patient-Reported Opioid Consumption and Pain Intensity After Common Orthopedic and Urologic Surgical Procedures With Use of an Automated Text Messaging System. JAMA Netw Open. 2021 Mar 1;4(3):e213243. doi: 10.1001/jamanetworkopen.2021.3243. PMID: 33764425. **- Not focused on an intervention of interest**

Ahonle ZJ, Jia H, Mudra SA, et al. Drug Overdose and Suicide Among Veteran Enrollees in the VHA: Comparison Among Local, Regional, and National Data. Fed Pract. 2020 Sep;37(9):420-5. doi: 10.12788/fp.0025. PMID: 33029067. **- Does not address an outcome of interest**

Al-Astal AY, Sodhi K, Lakhani HV. Optimization of Prescription Drug Monitoring Program to Overcome Opioid Epidemic in West Virginia. Cureus. 2022 Feb;14(2):e22434. doi: 10.7759/cureus.22434. PMID: 35371719. **- Narrative or scoping review**

Alderson SL, Farragher TM, Willis TA, et al. The effects of an evidence- and theory-informed feedback intervention on opioid prescribing for non-cancer pain in primary care: A controlled interrupted time series analysis. PLoS Med. 2021 Oct;18(10):e1003796. doi: 10.1371/journal.pmed.1003796. PMID: 34606504. **- Addresses effectiveness review question only but does not report clinical outcomes**

Alenezi A, Yahyouche A, Paudyal V. Interventions to optimize prescribed medicines and reduce their misuse in chronic non-malignant pain: a systematic review. Eur J Clin Pharmacol. 2021 Apr;77(4):467-90. doi: 10.1007/s00228-020-03026-4. PMID: 33123784. **- Not focused on an intervention of interest**

Alford DP, Zisblatt L, Ng P, et al. SCOPE of Pain: An Evaluation of an Opioid Risk Evaluation and Mitigation Strategy Continuing Education Program. Pain Med. 2016 Jan;17(1):52-63. doi: 10.1111/pme.12878. PMID: 26304703. **- Addresses implementation review question [6 and 7] but does not report clinical outcomes**

Alogaili F, Abdul Ghani N, Ahmad Kharman Shah N. Prescription drug monitoring programs in the US: A systematic literature review on its strength and weakness. J Infect Public Health. 2020 Oct;13(10):1456-61. doi: 10.1016/j.jiph.2020.06.035. PMID: 32694082. **- Intervention or policies established by entities other than healthcare providers**

Andereck J, Reuter Q, Kim HS, et al. Implementation of a novel audit and feedback program on discharge opioid prescribing. Academic emergency medicine. 2018;25:S52. doi: 10.1111/acem.13424. PMID: CN-01612744. **- Conference, meeting abstract, or poster**

Andereck JW, Reuter QR, Allen KC, et al. A Quality Improvement Initiative Featuring Peer-Comparison Prescribing Feedback Reduces Emergency Department Opioid Prescribing. Jt Comm J Qual Patient Saf. 2019 Oct;45(10):669-79. doi: 10.1016/j.jcjq.2019.07.008. PMID: 31488343. **- Addresses effectiveness review question only but does not report clinical outcomes**

Anne S, Mims JW, Tunkel DE, et al. Clinical Practice Guideline: Opioid Prescribing for Analgesia After Common Otolaryngology Operations Executive Summary. Otolaryngol Head Neck Surg. 2021 Apr;164(4):687-703. doi: 10.1177/0194599821996303. PMID: 33822678. **- Qualitative study without any quantitative data**

Arizmendez NP, Kotovicz F, Kram JJF, et al. Multimodal Local Opioid Prescribing Intervention Outcomes in Chronic Noncancer Pain Management. J Am Board Fam Med. 2019 Jul-Aug;32(4):559-66. doi: 10.3122/jabfm.2019.04.180296. PMID: 31300576. **- Addresses effectiveness review question only but does not report clinical outcomes**

Asamoah-Boaheng M, Badejo OA, Bell LV, et al. Interventions to Influence Opioid Prescribing Practices for Chronic Noncancer Pain: A Systematic Review and Meta-Analysis. Am J Prev Med. 2021 Jan;60(1):e15-e26. doi: 10.1016/j.amepre.2020.07.012. PMID: 33229143. **- Addresses effectiveness review question only but does not report clinical outcomes**

Ash N, Tuten J, Bohenek W, et al. A comprehensive approach to addressing the opioid epidemic in a large health system. Am J Health Syst Pharm. 2021 Feb 8;78(4):320-6. doi: 10.1093/ajhp/zxaa388. PMID: 33471051. **- Qualitative study without any quantitative data**

Aulet RM, Trieu V, Landrigan GP, et al. Changes in Opioid Prescribing Habits for Patients Undergoing Rhinoplasty and Septoplasty. JAMA Facial Plast Surg. 2019 Dec 1;21(6):487-90. doi: 10.1001/jamafacial.2019.0937. PMID: 31600382. **- Intervention or policies established by entities other than healthcare providers**

Awadalla R, Gnjidic D, Patanwala A, et al. The Effectiveness of Stewardship Interventions to Reduce the Prescribing of Extended-Release Opioids for Acute Pain: A Systematic Review. Pain Med. 2020 Oct 1;21(10):2401-11. doi: 10.1093/pm/pnaa139. PMID: 32488237. **- Addresses effectiveness review question only but does not report clinical outcomes**

Babino JM, Thornton JD, Putney K, et al. Evaluation of Discharge Opioid Prescribing in Coronary Artery Bypass Patients Following an Opioid Stewardship Intervention for Providers. J Pharm Pract. 2022 Apr 11:8971900221088797. doi: 10.1177/08971900221088797. PMID: 35410543. **- Addresses effectiveness review question only but does not report clinical outcomes**

Badreldin N, Ditosto JD, Holder K, et al. Interventions to Reduce Inpatient and Discharge Opioid Prescribing for Postpartum Patients: A Systematic Review. J Midwifery Womens Health. 2023 Mar;68(2):187-204. doi: 10.1111/jmwh.13475. PMID: 36811227. **- Addresses effectiveness review question only but does not report clinical outcomes**

Baird J, Faul M, Green TC, et al. Evaluation of a Safer Opioid Prescribing Protocol (SOPP) for Patients Being Discharged From a Trauma Service. J Trauma Nurs. 2019 May/Jun;26(3):113-20. doi: 10.1097/jtn.0000000000000435. PMID: 31483766. **- Addresses effectiveness review question only but does not report clinical outcomes**

Ball SJ, McCauley JA, Pruitt M, et al. Academic detailing increases prescription drug monitoring program use among primary care practices. J Am Pharm Assoc (2003). 2021 Jul-Aug;61(4):418-24.e2. doi: 10.1016/j.japh.2021.02.019. PMID: 33812783. **- Intervention or policies established by entities other than healthcare providers**

Barrett TW, McEvoy MD, Fowler LC, et al. Impact of an Asynchronous Spaced Education Learning Intervention on Emergency Medicine Clinician Opioid Prescribing. Cureus. 2021 Sep;13(9):e18165. doi: 10.7759/cureus.18165. PMID: 34707949. **- Addresses effectiveness review question only but does not report clinical outcomes**

Barth KS, Ball S, Adams RS, et al. Development and Feasibility of an Academic Detailing Intervention to Improve Prescription Drug Monitoring Program Use Among Physicians. J Contin Educ Health Prof. 2017 Spring;37(2):98-105. doi: 10.1097/ceh.0000000000000149. PMID: 28562498. **- Addresses implementation**

review question [6 and 7] but does not report clinical outcomes

Barth KS, Guille C, McCauley J, et al. Targeting practitioners: A review of guidelines, training, and policy in pain management. Drug Alcohol Depend. 2017 Apr 1;173 Suppl 1(Suppl 1):S22-s30. doi: 10.1016/j.drugalcdep.2016.08.641. PMID: 28363316. **- Systematic review published before 2019**

Baxter KJ, Short HL, Wetzel M, et al. Decreased opioid prescribing in children using an enhanced recovery protocol. J Pediatr Surg. 2019 Jun;54(6):1104-7. doi: 10.1016/j.jpedsurg.2019.02.044. PMID: 30885561. **- Not focused on an intervention of interest**

Beaudoin FL, Banerjee GN, Mello MJ. State-level and system-level opioid prescribing policies: The impact on provider practices and overdose deaths, a systematic review. J Opioid Manag. 2016 May-Jun;12(2):109-18. doi: 10.5055/jom.2016.0322. PMID: 27194195. **- Systematic review published before 2019**

Behar E, Bagnulo R, Coffin PO. Acceptability and feasibility of naloxone prescribing in primary care settings: A systematic review. Prev Med. 2018 Sep;114:79-87. doi: 10.1016/j.ypmed.2018.06.005. PMID: 29908763. **- Systematic review published before 2019**

Belavy DL, Tagliaferri SD, Buntine P, et al. Clinician education unlikely effective for guideline-adherent medication prescription in low back pain: systematic review and meta-analysis of RCTs. EClinicalMedicine. 2022 Jan;43:101193. doi: 10.1016/j.eclinm.2021.101193. PMID: 35028542. **- Addresses effectiveness review question only but does not report clinical outcomes**

Benavent KA, Altschul ND, Lincoln LF, et al. Patient Satisfaction and Opioid Use With a Postoperative Opioid Protocol After Common Hand Procedures. J Hand Surg Glob Online. 2020 Jul;2(4):191-5. doi: 10.1016/j.jhsg.2020.04.003. PMID: 35415503. **- No comparison group**

Bérubé M, Dupuis S, Leduc S, et al. Tapering Opioid Prescription Program for High-Risk Trauma Patients: A Pilot Randomized Controlled Trial. Pain Manag Nurs. 2022 Apr;23(2):142-50. doi: 10.1016/j.pmn.2021.08.001. PMID: 34479822. **- Non-USA based study or does not report data separately for USA**

Bestha D, Tomatsu S, Hutcheson B, et al. Impact of an opioid prescribing alert system on patients with posttraumatic stress disorder. Am J Addict. 2022 Mar;31(2):123-31. doi: 10.1111/ajad.13261. PMID: 35112432. **- Addresses effectiveness review question only but does not report clinical outcomes**

Billings JD, Huynh V, Leonard LD, et al. Addressing an epidemic: Improving guideline-concordant opioid prescribing in surgical patients. Surgery. 2022 Nov;172(5):1407-14. doi: 10.1016/j.surg.2022.06.033. PMID: 36088172. **- Addresses effectiveness review question only but does not report clinical outcomes**

Blaga V, Seth K, Valentim C, et al. Opioid Prescription in Ophthalmology and the Impact of a Decision Support Tool in Reducing Excess Dosing. Am J Ophthalmol. 2022 Nov;243:34-41. doi: 10.1016/j.ajo.2022.06.019. PMID: 35809659. **- Addresses effectiveness review question only but does not report clinical outcomes**

Bleicher J, Fender Z, Johnson JE, et al. Use of post-discharge opioid consumption patterns as a tool for evaluating opioid prescribing guidelines. Am J Surg. 2022 Jul;224(1 Pt A):58-63. doi: 10.1016/j.amjsurg.2021.12.020. PMID: 34973685. **- Not focused on an intervention of interest**

Bleicher J, Stokes SM, Brooke BS, et al. Patient-centered Opioid Prescribing: Breaking Away From One-Size-Fits-All Prescribing Guidelines. J Surg Res. 2021 Aug;264:1-7. doi: 10.1016/j.jss.2021.01.048. PMID: 33744772. **- Addresses effectiveness review question only but does not report clinical outcomes**

Blind F, Melton J, Karp J, et al. Evaluation of the use of individualized patient care plans in frequent emergency department visitors with pain complaints. Int J Emerg Med. 2022 Aug 22;15(1):37. doi: 10.1186/s12245-022-00440-6. PMID: 35996083. **- Addresses effectiveness review question only but does not report clinical outcomes**

Bloom DA, Manjunath AK, Gualtieri AP, et al. Patient Satisfaction After Total Hip Arthroplasty Is Not Influenced by Reductions in Opioid Prescribing. J Arthroplasty. 2021 Jul;36(7s):S250-s7. doi: 10.1016/j.arth.2021.02.009. PMID: 33640183. **- Not focused on an intervention of interest**

Bohnert ASB, Guy GP, Jr., Losby JL. Opioid Prescribing in the United States Before and After the Centers for Disease Control and Prevention's 2016 Opioid Guideline. Ann Intern Med. 2018 Sep 18;169(6):367-75. doi: 10.7326/m18-1243. PMID: 30167651. **- Addresses effectiveness review question only but does not report clinical outcomes**

Bongiovanni T, Hansen K, Lancaster E, et al. Adopting best practices in post-operative analgesia prescribing in a safety-net hospital: Residents as a conduit to change. Am J Surg. 2020 Feb;219(2):299-303. doi: 10.1016/j.amjsurg.2019.12.023. PMID: 31928779. **- Addresses effectiveness review question only but does not report clinical outcomes**

Booth D, Amalfitano C, Forestine A. Changes in Opioid Prescription Rates at Discharge After Targeted Provider Education in the Emergency Department. J Pharm Pract. 2022 Nov 13:8971900221131911. doi: 10.1177/08971900221131911. PMID: 36373419. **- Addresses effectiveness review question only but does not report clinical outcomes**

Boren LL, Locke AM, Friedman AS, et al. Team-Based Medicine: Incorporating a Clinical Pharmacist into Pain and Opioid Practice Management. Pm r. 2019 Nov;11(11):1170-7. doi: 10.1002/pmrj.12127. PMID: 30729723. - **Other: Study included in previous systematic reviews**

Borrelli EP, Bratberg J, Hallowell BD, et al. Application of a diazepam milligram equivalency algorithm to assess benzodiazepine dose intensity in Rhode Island in 2018. J Manag Care Spec Pharm. 2022 Jan;28(1):58-68. doi: 10.18553/jmcp.2022.28.1.58. PMID: 34949119. **- Not focused on an intervention of interest**

Bossenbroek Fedoriw K, Prentice A, Slatkoff S, et al. A Systematic Approach to Opioid Prescribing. J Am Board Fam Med. 2020 Nov-Dec;33(6):992-7. doi: 10.3122/jabfm.2020.06.190463. PMID: 33219078. **- Addresses effectiveness review question only but does not report clinical outcomes**

Bourgeois HC, Proteau RC, Vielma CV, et al. Evaluation of an Interdisciplinary Controlled Substance Review Committee on Opioid Prescribing in a Community Health Center. Pain Med. 2020 Sep 1;21(9):1840-6. doi: 10.1093/pm/pnaa075. PMID: 32289825. **- Addresses effectiveness review question only but does not report clinical outcomes**

Boyle KL, Cary C, Dizitzer Y, et al. Reduction of opioid prescribing through the sharing of individual physician opioid prescribing practices. Am J Emerg Med. 2019 Jan;37(1):118-22. doi: 10.1016/j.ajem.2018.09.052. PMID: 30343961. **- Addresses effectiveness review question only but does not report clinical outcomes**

Brandal D, Keller MS, Lee C, et al. Impact of Enhanced Recovery After Surgery and Opioid-Free Anesthesia on Opioid Prescriptions at Discharge From the Hospital: A Historical-Prospective Study. Anesth Analg. 2017 Nov;125(5):1784-92. doi: 10.1213/ane.0000000000002510. PMID: 29049123. **- Other: ERAS pathway**

Brar S, Aujla S, Tang S, et al. Impact of a Clinical Intervention to Decrease Opioid Prescribing in a Post-Cesarean Delivery. J Obstet Gynaecol Can. 2022 Apr;44(4):398-402. doi: 10.1016/j.jogc.2021.11.009. PMID: 34848352. **- Non-USA based study or does not report data separately for USA**

Bredemeyer M. CDC Develops Guideline for Opioid Prescribing. Am Fam Physician. 2016 Jun 15;93(12):1042-3. PMID: 27304778. **- No original data (opinion, descriptive data, letters, editorial, commentary)**

Breeden MA, Jacobs CK, Witthaus M, et al. Prescribing Patterns and Use of Risk-Reduction Tools After Implementing an Opioid-Prescribing Protocol. J Am Board Fam Med. 2020 Jan-Feb;33(1):27-33. doi: 10.3122/jabfm.2020.01.190247. PMID: 31907243. **- Addresses effectiveness review question only but does not report clinical outcomes**

Brose SW, Schneck H, Bourbeau DJ. An Interdisciplinary Approach to Reducing Opioid Prescriptions to Patients with Chronic Pain in a Spinal Cord Injury Center. Pm r. 2019 Feb;11(2):135-41. doi: 10.1016/j.pmrj.2018.09.030. PMID: 30266347. **- Addresses effectiveness review question only but does not report clinical outcomes**

Burns S, Urman R, Pian R, et al. Reducing New Persistent Opioid Use After Surgery: A Review of Interventions. Curr Pain Headache Rep. 2021 Mar 24;25(5):27. doi: 10.1007/s11916-021-00943-6. PMID: 33760983. **- Narrative or scoping review**

Buttorff C, Trujillo AJ, Castillo R, et al. The impact of practice guidelines on opioid utilization for injured workers. Am J Ind Med. 2017 Dec;60(12):1023-30. doi: 10.1002/ajim.22779. PMID: 28990210. **- Addresses effectiveness review question only but does not report clinical outcomes**

Calcaterra SL, Butler M, Olson K, et al. The Impact of a PDMP-EHR Data Integration Combined With Clinical Decision Support on Opioid and Benzodiazepine Prescribing Across Clinicians in a Metropolitan Area. J Addict Med. 2022 May-Jun 01;16(3):324-32. doi: 10.1097/adm.0000000000000905. PMID: 34392255. **- Addresses effectiveness review question only but does not report clinical outcomes**

Calderon T, Hedges E, Livingston MH, et al. Opioid stewardship in pediatric surgery: Approaching zero. J Pediatr Surg. 2021 Mar;56(3):573-9. doi: 10.1016/j.jpedsurg.2020.08.035. PMID: 33008639. **- Not focused on an intervention of interest**

Carey CM, Meille G, Buchmueller TC. Provider Compliance With Kentucky's Prescription Drug Monitoring Program's Mandate To Query Patient Opioid History. Health Aff (Millwood). 2021 Mar;40(3):461-8. doi: 10.1377/hlthaff.2020.01316. PMID: 33646863. **- Intervention or policies established by entities other than healthcare providers**

Carlile N, Fuller TE, Benneyan JC, et al. Lessons Learned in Implementing a Chronic Opioid Therapy Management System. J Patient Saf. 2022 Dec 1;18(8):e1142-e9. doi: 10.1097/pts.0000000000001039. PMID: 35617623. **- Addresses implementation review question [6 and 7] but does not report clinical outcomes**

Carlson A, Nelson ME, Patel H. Longitudinal impact of a pre-populated default quantity on emergency department opioid prescriptions. J Am Coll Emerg Physicians Open. 2021 Feb;2(1):e12337. doi: 10.1002/emp2.12337. PMID: 33521788. **- Addresses effectiveness review question only but does not report clinical outcomes**

Caruso TJ, Trivedi S, Chadwick W, et al. A Quality Improvement Project to Reduce Combination Acetaminophen-opioid Prescriptions to Pediatric Orthopedic Patients. Pediatr Qual Saf. 2020 May-Jun;5(3):e291. doi: 10.1097/pq9.0000000000000291. PMID: 32607456. **- Addresses effectiveness review question only but does not report clinical outcomes**

Castillo-Carniglia A, González-Santa Cruz A, Cerdá M, et al. Changes in opioid prescribing after implementation of mandatory registration and proactive reports within California's prescription drug monitoring program. Drug Alcohol Depend. 2021 Jan 1;218:108405. doi: 10.1016/j.drugalcdep.2020.108405. PMID: 33234299. **- Does not address an outcome of interest**

Cedillo G, George MC, Deshpande R, et al. Toward Safer Opioid Prescribing in HIV care (TOWER): a mixed-methods, cluster-randomized trial. Addict Sci Clin Pract. 2022 May 16;17(1):28. doi: 10.1186/s13722-022-00311-8. PMID: 35578356. **- Does not meet sample size criteria**

Centers For Disease C, Prevention Public Health Service USDOH, Human S. Guideline for Prescribing Opioids for Chronic Pain. J Pain Palliat Care Pharmacother. 2016 Jun;30(2):138-40. doi: 10.3109/15360288.2016.1173761. PMID: 27301691. **- No original data (opinion, descriptive data, letters, editorial, commentary)**

Ceuppens C, Dudi-Venkata NN, Lee YD, et al. Feasibility study of an online modifiable Enhanced Recovery After Surgery protocol with specific focus on opioid avoidance. ANZ J Surg. 2020 Oct;90(10):1947-52. doi:

10.1111/ans.15976. PMID: 32407004. - **Not focused on an intervention of interest**

Chan KY, Keogh S, Aucharaz N, et al. Opioid prescribing after breast surgery: A systematic review of guidelines. Surgeon. 2022 Dec 31doi: 10.1016/j.surge.2022.12.004. PMID: 36593160. - **Does not address an outcome of interest**

Chandrasekar T, Glick L, Wong D, et al. Simple frameshifts in minimally invasive surgery postoperative pain management significantly reduce opiate prescriptions. Can J Urol. 2020 Jun;27(3):10250-6. PMID: 32544049. - **Other: Study included in previous systematic reviews**

Chen A, Legal M, Shalansky S, et al. Evaluating a Pharmacist-Led Opioid Stewardship Initiative at an Urban Teaching Hospital. Can J Hosp Pharm. 2021 Summer;74(3):248-55. doi: 10.4212/cjhp.v74i3.3152. PMID: 34248165. - **Non-USA based study or does not report data separately for USA**

Chen AMH, Gardner J, Wandling E, et al. The impact of a provider motivational interviewing-based training on chronic pain management in a federally-qualified health center. Res Social Adm Pharm. 2022 Oct;18(10):3839-45. doi: 10.1016/j.sapharm.2022.04.001. PMID: 35400614. - **Does not meet sample size criteria**

Chen JH, Hom J, Richman I, et al. Effect of opioid prescribing guidelines in primary care. Medicine (Baltimore). 2016 Aug;95(35):e4760. doi: 10.1097/md.0000000000004760. PMID: 27583928. - **Other: Study included in previous systematic reviews**

Childs E, Tano CA, Mikosz CA, et al. Factors That Affect Opioid Quality Improvement Initiatives in Primary Care: Insights from Ten Health Systems. Jt Comm J Qual Patient Saf. 2023 Jan;49(1):26-33. doi: 10.1016/j.jcjq.2022.10.002. PMID: 36443166. - **Addresses implementation review question [6 and 7] but does not report clinical outcomes**

Chinman M, Gellad WF, McCarthy S, et al. Protocol for evaluating the nationwide implementation of the VA Stratification Tool for Opioid Risk Management (STORM). Implement Sci. 2019 Jan 18;14(1):5. doi: 10.1186/s13012-019-0852-z. PMID: 30658658. - **No original data (opinion, descriptive data, letters, editorial, commentary)**

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Tsega S, Hernandez-Meza G, DiRisio AC, et al. A Multifaceted, Student-Led Approach to Improving the Opioid Prescribing Practices of Hospital Medicine Clinicians. Jt Comm J Qual Patient Saf. 2020 Mar;46(3):153-7. doi: 10.1016/j.jcjq.2019.11.006. PMID: 31899157. **- Addresses effectiveness review question only but does not report clinical outcomes**

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Opioid Prescribing at a Children's Hospital. Clin Pediatr (Phila). 2022 Jul;61(7):465-8. doi: 10.1177/00099228221085344. PMID: 35442096. **- Addresses effectiveness review question only but does not report clinical outcomes**

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Wood D, Moy SF, Zhang S, et al. Impact of a prescriber and patient educational intervention on discharge analgesia prescribing and hospital readmission rates following elective unilateral total hip and knee arthroplasty. BMJ Open Qual. 2022 Aug;11(3)doi: 10.1136/bmjoq-2021-001672. PMID: 35914816. **- Non-USA based study or does not report data separately for USA**

Wood S, Foy R, Willis TA, et al. General practice responses to opioid prescribing feedback: a qualitative process evaluation. Br J Gen Pract. 2021 Oct;71(711):e788-e96. doi: 10.3399/bjgp.2020.1117. PMID: 33979300. **- Qualitative study without any quantitative data**

Xie CX, Chen Q, Hincapié CA, et al. Effectiveness of clinical dashboards as audit and feedback or clinical decision support tools a systematic literature review. Transl Behav Med. 2021 Aug 13;11(8):1481-94. doi: 10.1093/tbm/ibab007. PMID: 33677606. **- Not focused on an intervention of interest**

on medication use and test ordering: a systematic review of randomized controlled trials. J Am Med Inform Assoc. 2022 Sep 12;29(10):1773-85. doi: 10.1093/jamia/ocac094. PMID: 35689652. **- Not focused on an intervention of interest**

Yanik JM, Glass NA, Caldwell LS, et al. A Novel Prescription Method Reduces Postoperative Opioid Distribution and Consumption: A Randomized Clinical Trial. Hand (N Y). 2022 Jun 3:15589447221096709. doi: 10.1177/15589447221096709. PMID: 35656851. **- Does not meet sample size criteria**

Yorkgitis BK, Garbas B, Cole D. Opioid Prescribing Education for Physician Assistant Students: A Physician Assistant Educator Survey. J Physician Assist Educ. 2019 Mar;30(1):27-33. doi: 10.1097/jpa.0000000000000238. PMID: 30720704. **- Addresses implementation review question [6 and 7] but does not report clinical outcomes**

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Young LS, Crausman RS, Fulton JP. Suboptimal Opioid Prescribing: A Practice Change Project. R I Med J (2013). 2018 Mar 1;101(2):41-4. PMID: 29490325. **- Addresses effectiveness review question only but does not report clinical outcomes**

Zaman T, Rife TL, Batki SL, et al. An electronic intervention to improve safety for pain patients co-prescribed chronic opioids and benzodiazepines. Subst Abus. 2018;39(4):441-8. doi: 10.1080/08897077.2018.1455163. PMID: 29595408. - **Other: Study included in previous systematic reviews**

Zavaleta KW, Philpot LM, Cunningham JL, et al. Why we still prescribe so many opioids: A qualitative study on -barriers and facilitators to prescribing guideline implementation. J Opioid

Manag. 2021 Mar-Apr;17(2):115-24. doi: 10.5055/jom.2021.0622. PMID: 33890275. **- Qualitative study without any quantitative data**

Zgierska AE, Robinson JM, Lennon RP, et al. Increasing system-wide implementation of opioid prescribing guidelines in primary care: findings from a non-randomized stepped-wedge quality improvement project. BMC Fam Pract. 2020 Nov 28;21(1):245. doi: 10.1186/s12875-020-01320-9. PMID: 33248458. **- Addresses effectiveness review question only but does not report clinical outcomes**

Zhang DDQ, Dossa F, Arora A, et al. Recommendations for the Prescription of Opioids at Discharge After Abdominopelvic Surgery: A Systematic Review. JAMA Surg. 2020 May 1;155(5):420-9. doi: 10.1001/jamasurg.2019.5875. PMID: 32159738. **- Does not address an outcome of interest**

Zhang IY, Wong ES, Rosen JE, et al. Association Between Statewide Medicaid Opioid Policy and Postoperative Opioid Prescribing among Surgeons at a Large Safety-Net Hospital. J Am Coll Surg. 2022 Sep 1;235(3):519-28. doi: 10.1097/xcs.0000000000000274. PMID: 35972173. **- Addresses effectiveness review question only but does not report clinical outcomes**

Ziegelmann M, Joseph J, Glasgow A, et al. Comparison of prescribing patterns before and after implementation of evidence-based opioid prescribing guidelines for the postoperative urologic surgery patient. Am J Surg. 2020 Aug;220(2):499-504. doi: 10.1016/j.amjsurg.2019.11.037. PMID: 31831158. **- Addresses effectiveness review question only but does not report clinical outcomes**

Zimbro KS, Maduro RS, Haimani OF, et al. Women RISE: Empowering Women to Manage Chronic Pain and Informing Provider Opioid Prescribing Practices. J Nurs Care Qual. 2021 Oct-Dec 01;36(4):315-21. doi: 10.1097/ncq.0000000000000559. PMID: 33734185. **- Addresses effectiveness review question only but does not report clinical outcomes**

Zivin K, White JO, Chao S, et al. Implementing Electronic Health Record Default Settings to Reduce Opioid Overprescribing: A Pilot Study. Pain Med. 2019 Jan 1;20(1):103-12. doi: 10.1093/pm/pnx304. PMID: 29325160. **- Addresses effectiveness review question only but does not report clinical outcomes**

Zolin SJ, Ho VP, Young BT, et al. Opioid prescribing in minimally injured trauma patients: Effect of a state prescribing limit. Surgery. 2019 Oct;166(4):593-600. doi: 10.1016/j.surg.2019.05.040. PMID: 31326187. **- Intervention or policies established by entities other than healthcare providers**

Zorrilla-Vaca A, Rice D, Brown JK, et al. Sustained reduction of discharge opioid prescriptions in an enhanced recovery after thoracic surgery program: A multilevel generalized linear model. Surgery. 2022 Feb;171(2):504-10. doi: 10.1016/j.surg.2021.08.039. PMID: 34740455. **- Interventions focusing on treatment of opioid use disorder**

Appendix C. Evidence Tables

[Reference list located at the end of the body of the report]

Evidence Table C-1. Characteristics of included systematic reviews addressing harms, effectiveness and unintended effects of opioid stewardship practices

Author, Year	Objective	Combined Search/Study design	Population	Setting
Avery, 2022[14]	Review interventions to reduce long term opioid treatment in people with chronic noncancer pain.	Search date: up to July 2021 Included studies, n: 36 RCTs = 27 Non-RCTs = 5 Observational = 0 Other: Uncontrolled studies n=4	Adults with chronic pain, prescribed opioid treatment for pain management. Included studies on people not using opioids for non-medical reasons, patients without cancer or not HIV positive.	Only included studies where patients are not in hospice only or palliative care only.

Author, Year	Objective	Combined Search/Study design	Population	Setting
Carnes, 2022[15]	Review of the effectiveness of various types of interventions in reducing opioid prescriptions after urological surgery.	Search date: up to January 2021 Included studies, n: 22 RCTs = 0 Non-RCTs = 0 Observational = 22 Other: NA	Adult patients receiving outpatient opioid prescription after urological surgery	Outpatient setting.

Author, Year	Objective	Combined Search/Study design	Population	Setting
Haegerich, 2019[16]	Provides a recent synthesis on the effectiveness of prevention strategies that address prescription and illicit opioid overdose.	Search date: January 2013 to May 2018 Included studies, n: 251 RCTs = 32 Non-RCTs = 5 Observational = 155 Other: Non-comparative study n=59	Included human studies only and studies not evaluating of abuse-deterrents, opioid use disorder, or compulsory drug treatments.	Included studies where the interventions were not implemented in correctional settings.
Hopkins, 2019[17]	Identify the objective impacts of education interventions on opioid prescribing in the acute care setting.	Search date: up to December 2018 Included studies, n: 9 RCTs = 0 Non-RCTs = 0 Observational = 9 Other: NA	Intervention targeting patients in acute setting only.	All studies in an acute setting except those focusing on palliative care.
Iqbal, 2022[18]	Assess the effectiveness of interventions delivered by pharmacists in outpatient clinical settings, community pharmacies and primary care services in optimizing opioid therapy for people with chronic non-malignant pain and to explore stakeholders' opinions about role of pharmacists in optimizing opioid therapy.	Search date: January 1990 to June 2020 Included studies, n: 14 RCTs = 1 Non-RCTs = 2 Observational = 8 Other: Quasi-experimental n=1, qualitative n=2	Adult patients with chronic pain with duration longer than 3 months, pain treated with opioids. In addition, patients with no opioid addiction or abuse, and no illicit opioid use.	Outpatient care, non-palliative care.

Author, Year	Objective	Combined Search/Study design	Population	Setting
Kadakia, 2020[19]	Evaluate the impact of prescription opioid-related education provided to a patient by a healthcare provider on patient outcomes.	Search date: 1996 to October 2018 Included studies, n: 10 RCTs = NR Non-RCTs = NR Observational = NR Other: NA	Adult patients undergoing educational intervention targeting opioid medication	Only studies that explore provider-initiated education interventions taking place outside the United States
Langford, 2023[20]	Synthesize and evaluate evidence from systematic reviews examining the effectiveness and outcomes of patient-targeted opioid deprescribing interventions for all types of pain	Search date: August 2011 to August 2021 Included studies, n: 12 RCTs = 0 Non-RCTs = 0 Observational = 0 Other: Systematic reviews n=12	Systematic reviews of any primary study design with or without meta-analyses	NA
Liu, 2020[21]	Summarize the effectiveness of interventions on appropriate opioid use for noncancer pain among hospital inpatients.	Search date: 1960 to March 2018 Included studies, n: 37 RCTs = 4 Non-RCTs = 0 Observational = 31 Other: Cross-sectional n=2	Adults with noncancer pain and studies on focusing on discharge opioid use	Quantitative outcomes of interventions on appropriate opioid use for noncancer pain during inpatient stay or ED visit. Opioid use not related to palliative care, oncology, or opioid substitution therapy

Author, Year	Objective	Combined Search/Study design	Population	Setting
Lovecchio, 2019[22]	Evaluate institutional strategies that reduce opioid administration or consumption after orthopedic surgery	Search date: up to October 2018 Included studies, n: 13 RCTs = 1 Non-RCTs = 0 Observational = 11 Other: Review with meta-analysis n=1	Surgical patients	Interventions by hospital staff to reduce post-operative opioid use or opioid prescription amounts after surgery
Phinn, 2023[23]	Aims to summarize the effectiveness of organizational interventions on appropriate opioid prescribing for noncancer pain upon hospital discharge	Search date: 2011 - March 2021 Included studies, n: 43 RCTs = 3 Non-RCTs = 0 Observational = 38 Other: Time series n=2	Adult patients 18 or over years of age, patients prescribed opioids for noncancer pain upon hospital discharge. Patients not prescribed opioids for palliative care, oncology/cancer pain or opioid-substitution therapy.	NA
Raoul, 2022[24]	Review and analyze interventions designed to reduce the rate of opioid prescriptions or the quantity prescribed for pain in adults discharged from the emergency department.	Search date: up to March 2021 Included studies, n: 63 RCTs = 1 Non-RCTs = 0 Observational = 39 Other: Time series n=21, cohort n=2	Adults discharged from emergency department for home pain management.	Patients discharged from the emergency department

Author, Year	Objective	Combined Search/Study design	Population	Setting
Wong, 2020[25]	Synthesized the available evidence on interventional strategies to improve care-associated outcomes for frequent ED utilizers with chronic noncancer pain.	Search date: Up to June 2018 Included studies, n: 13 RCTs = 4 Non-RCTs = 0 Observational = 9 Other: NA	Adult patients identified by the study investigators as frequent ED utilizers	NA
Zhang, 2020[26]	Summarize strategies to reduce postsurgical opioid prescribing at discharge.	Search date: Up to December 2018 Included studies, n: 24 RCTs = 1 Non-RCTs = 0 Observational = 22 Other: Interrupted time series n=1	Adults undergoing any surgery	Studies not evaluating policy level interventions
Zorrilla-Vaca, 2022[27]	Evaluates the impact of perioperative opioid education on postoperative opioid consumption patterns including opioid cessation, number of pills consumed, and opioid prescription refills.	Search date: up to September 2020 Included studies, n: 11 RCTs = 11 Non-RCTs = 0 Observational = 0 Other: NA	Adult patients undergoing surgery	Intervention conducted during hospitalization either before or after surgery

ED = emergency department; NA = not available; NR = not reported; RCT = randomized controlled trial

Evidence Table C-2. Results of included systematic reviews addressing harms, effectiveness and unintended effects of organizational leadership and policies within a healthcare facility or healthcare system

Author, Year	Intervention	Outcome Category	Results
Haegerich, 2019[16]	Clinical guideline implementation	Rates of opioid prescribing or ordering	Significant decrease in rate of opioid prescriptions at national and state level (specifically, Washington state)
Haegerich, 2019[16]	Providing decision support at the point of care	Healthcare utilization (focusing on emergency department use and hospitalizations for adverse events)	Decrease in ED visits
Haegerich, 2019[16]	Providing decision support at the point of care	Rates of opioid prescribing or ordering	Shown to reduce opioid prescribing after intervention
Liu, 2020[21]	Computerized physician order entry	Adverse consequences	Decrease in adverse drug events incidence overall (34.7 vs 23.3%) and respiratory depression (16.7 vs 8.3%)
Lovecchio, 2019[22]	Pain management protocol for orthopedic nurses	Rates of nonopioid analgesic prescribing	Increase in patients receiving opioid and nonopioid analgesics (38.8% pre vs 66.2% post-intervention)
Lovecchio, 2019[22]	Prescribing guidelines	Opioid refill requests	Comparable refill rates between arms or was not changed post intervention
Lovecchio, 2019[22]	Prescribing guidelines	Patient satisfaction	High satisfaction in both cohorts in one study
Lovecchio, 2019[22]	Prescribing guidelines	Rates of opioid prescribing or ordering	Significantly reduced mean prescription amounts
Lovecchio, 2019[22]	Prescribing guidelines	Total MME per prescription or per patient	Number of pills per prescription decreased
Phinn, 2023[23]	Changes to default quantities in electronic medical records	Rates of opioid prescribing or ordering	Two studies showed decrease in opioid tablets prescribed (25 to 40% reduction), one study showed no significant change.
Phinn, 2023[23]	Employed multimodal analgesia guidelines using paracetamol, gabapentin, naproxen and celecoxib as first-line choices for pain management	Pain intensity or distress	Decrease in mean postoperative Defense and Veterans Pain Rating Scale (DVPRS) pain scores between control vs enhanced recovery after surgery (ERAS) groups: 4.2 (SD 1.6) vs 2.9 (SD 2.1), p=0.042
Phinn, 2023[23]	Employed multimodal analgesia guidelines using paracetamol, gabapentin, naproxen and celecoxib as first-line choices for pain management	Pain intensity or distress	No change in postoperative phone calls for uncontrolled pain
Phinn, 2023[23]	Employed multimodal analgesia guidelines using paracetamol, gabapentin, naproxen and celecoxib as first-line choices for pain management	Rates of opioid prescribing or ordering	Decrease of 36 to 93% in the proportion of patients discharged with an opioid. Also decrease of 26% in the quantity of opioids prescribed per patient discharge.

Author, Year	Intervention	Outcome Category	Results
Phinn, 2023[23]	Implemented "general" prescribing guidelines	Rates of opioid prescribing or ordering	Decrease in the proportion of patients prescribed opioids on discharge of 16–36% and a relative decrease in the number of opioid tablets per prescription of 15%
Phinn, 2023[23]	Implementing procedure-specific guidelines, where the expected pain from the procedure guided the amount of opioids prescribed	Patient satisfaction	No change in median patient satisfaction with pain control after discharge using Likert scale: 9 (IQR 8–10) to 9 (IQR 8–10); p=0.87
Raoul, 2022[24]	Electronic medical record quantity changes	Rates of opioid prescribing or ordering	Pre-post and cohort studies: reduced rate of opioid prescription, OR 0.94 (95% CI: 0.88 to 0.99)
Raoul, 2022[24]	Electronic medical record quantity changes	Total MME per prescription or per patient	Interrupted time series studies: reduced rate of opioid prescription at 6 months, change -11.65 (95% CI: -29.30 to 5.99) Pre-post/cohort studies: reduced rate of opioid prescription quantity, SMD -0.20 (95% CI: -0.47 to 0.07)
Zhang, 2020[26]	Decreased the default number of opioid pills within an electronic medical record system	Opioid refill requests	No significant increase in the proportion of prescription refill in one study (1.5% to 3.0%, p=0.41)
Zhang, 2020[26]	Decreased the default number of opioid pills within an electronic medical record system	Total MME per prescription or per patient	Mean of 34.4 MMEs were prescribed less per patient (95% CI, 27.5–41.4) in one study
Zhang, 2020[26]	Institutional opioid prescribing recommendations developed through local consensus	Opioid refill requests	Differing effect on opioid refills. 3 studies showed no significant effect, and two studies showed significantly increased opioid refills or requests (6.6% postintervention vs 0.8% preintervention, p=0.01; 28.7% on-protocol patients vs 18.9% off-protocol patients, p=0.001)
Zhang, 2020[26]	Institutional opioid prescribing recommendations developed through local consensus	Pain intensity or distress	Majority of studies did not demonstrate any increase in postoperative pain associated with a reduced amount of opioid* prescribed. However, there was evidence that postoperative pain was inadequately controlled in 3 studies.
Zhang, 2020[26]	Institutional opioid prescribing recommendations developed through local consensus	Number of pills per prescription	Majority of studies describing a local opioid prescribing consensus reported a decrease in the mean amount of opioid* prescribed at discharge immediately after the intervention

CI = confidence interval; ED = emergency department; IQR = interquartile range; MME = morphine milligram equivalent; OR = odds ratio; SD = standard deviation; SMD=standardized mean deviation

*"amount of opioids" when used in these studies means "number or amount of pills"

Evidence Table C-3. Results of included systematic reviews addressing harms, effectiveness and unintended effects of clinical knowledge, expertise, and behavior interventions related to prescribed or ordered opioids

Author, Year	Intervention	Outcome Category	Results
Avery, 2022[14]	Deprescription methods (defined as patient or prescriber focused interventions, may or may not include alternative pain management techniques)	Total MME per prescription or per patient	A small effect on opioid dose, mean difference –6.8 mg (SE 1.6) oral morphine equivalent, P<0.001; adjusted OR for dose reduction 1.6, 95% CI: 1.1 to 2.4; moderate level certainty), based on 1 RCT
Avery, 2022[14]	Opioid replacement treatment (defined as transition to maintenance therapy and then weaning off)	Total MME per prescription or per patient	Showed no significant difference between treatment groups reported for opioid dose, based on 5 RCTs, no meta-analysis done.
Haegerich, 2019[16]	Procedures for developing coordinated recommendations for opioid prescribing	Rates of opioid prescribing or ordering	Shown to reduce opioid prescribing after intervention
Haegerich, 2019[16]	Provider education	Rates of opioid prescribing or ordering	A larger decrease in opioid prescribing from physicians in the intervention group vs those in the control in one RCT. Other studies showed increased knowledge led to significant changes in prescribing behavior.
Hopkins, 2019[17]	Provider education to optimize opioid prescribing in an acute setting	Opioid refill requests	Two studies examined refill requests did not detect an increase in refill requests
Hopkins, 2019[17]	Provider education to optimize opioid prescribing in an acute setting	Pain intensity or distress	One study reported no increase in pain-related complaints after intervention
Hopkins, 2019[17]	Provider education to optimize opioid prescribing in an acute setting	Number of pills per prescription	Two studies showed a significant reduction in number of pills supplied with a reduction of 53% in one study.
Hopkins, 2019[17]	Provider education to optimize opioid prescribing in an acute setting	Rates of nonopioid analgesic prescribing	One study demonstrated a nonsignificant increase in the total proportion of patients discharged without opioids (9% to 12.7%; P = 0.08)
Hopkins, 2019[17]	Provider education to optimize opioid prescribing in an acute setting	Rates of opioid prescribing or ordering	One study showed no difference in overall prescriptions written after intervention, while another study showed a significant reduction.
Hopkins, 2019[17]	Provider education to optimize opioid prescribing in an acute setting	Total MME per prescription or per patient	5 studies reported significant reduction in total dosage and quantity of opioid medication supplied on discharge after intervention

Author, Year	Intervention	Outcome Category	Results
Iqbal, 2022[18]	Intervention by pharmacist, generally a detailed review of patient charts	Pain intensity or distress	5 studies showed significant reduction in pain intensity. 3 studies showed no significant decrease in pain intensity
Iqbal, 2022[18]	Intervention by pharmacist, generally a detailed review of patient charts	Barriers	Gaps in communications with PCPs
Iqbal, 2022[18]	Intervention by pharmacist, generally a detailed review of patient charts	Barriers	Inadequate monitoring from pharmacists due to lack of access to patient medical information,
Iqbal, 2022[18]	Intervention by pharmacist, generally a detailed review of patient charts	Barriers	Lack of a comprehensive approach by utilizing skillset of all members of healthcare team
Iqbal, 2022[18]	Intervention by pharmacist, generally a detailed review of patient charts	Barriers	Pharmacists feel less confident due to lack of specialized education and training
Iqbal, 2022[18]	Intervention by pharmacist, generally a detailed review of patient charts	Referrals relevant to pain management (behavioral health, physical therapy, etc.)	Increased referrals to physical therapy in 1 study
Iqbal, 2022[18]	Intervention by pharmacist, generally a detailed review of patient charts	Rates of nonopioid analgesic prescribing	1 study showed an increase of nonopioid analgesics.
Iqbal, 2022[18]	Intervention by pharmacist, generally a detailed review of patient charts	Total MME per prescription or per patient	5 studies showed reduction in overall opioid dose after pharmacist intervention. 1 study showed an increase in opioid dose.
Lovecchio, 2019[22]	Educational program on opioid prescribing for surgical interns	Total MME per prescription or per patient	Median MME prescribed per procedure was unchanged by program,
Phinn, 2023[23]	Education on appropriate opioid prescribing, guidelines, and decision-making tools	Rates of nonopioid analgesic prescribing	Increase of 93% in the number of nonopioid analgesic prescriptions in one study
Phinn, 2023[23]	Education on appropriate opioid prescribing, guidelines, and decision-making tools	Rates of opioid prescribing or ordering	Decrease of up to 20-47% in the proportion of patients discharged with an opioid.
Phinn, 2023[23]	Educational program on opioid prescribing for surgical interns	Healthcare utilization (focusing on emergency department use and hospitalizations for adverse events)	Increase in number of patients with return visits to ED within 30 days for pain control after surgical procedure or previous ED visit post-intervention; p=NR

Author, Year	Intervention	Outcome Category	Results
Phinn, 2023[23]	Implementing procedure-specific guidelines, where the expected pain from the procedure guided the amount of opioids* prescribed	Rates of opioid prescribing or ordering	Decrease in the quantity of opioids (tabs, MME, OME) prescribed by 20 to 44%
Phinn, 2023[23]	The amount of opioids* consumed during the 24–48 hours prior to discharge to guide prescription quantities	Rates of opioid prescribing or ordering	Decrease in the quantity of opioids (tabs, MME, OME) prescribed by 31 to 56%
Zhang, 2020[26]	Educational meetings: educating surgical interns regarding postoperative prescribing	Total MME per prescription or per patient	Significant reduction in the amount of opioid* per prescription by 83.0 MMEs (95% CI, 51.8–115.8) (pre-post comparison) in one study
Zhang, 2020[26]	Opioid-free prescription, often including multimodal analgesia	Opioid refill requests	No statistically significant change in requirement for additional prescriptions in one pre-post study
Zhang, 2020[26]	Opioid-free prescription, often including multimodal analgesia	Pain intensity or distress	No statistically significant change in pain scores in 3 observational studies
Zhang, 2020[26]	Opioid-free prescription, often including multimodal analgesia	Patient satisfaction	No statistically significant change in patient satisfaction in one pre-post study
Zhang, 2020[26]	Pharmacist assistance in prescription preparation	Healthcare utilization (focusing on emergency department use and hospitalizations for adverse events)	No increase in hospital visit for postoperative pain was observed after the intervention
Zhang, 2020[26]	Pharmacist assistance in prescription preparation	Total MME per prescription or per patient	Average amount of opioid* prescribed per patient decreased by 110.3 MMEs (95% CI 90.8, 129.0)

CI = confidence interval; ED = emergency department; mg = milligram; MME = morphine milligram equivalent; NR = not reported; OME = oral morphine equivalents; OR = odds ratio; PCP = primary care provider; RCT = randomized controlled trial; SE = standard error; tabs = tablets

*"amount of opioids" when used in these studies means "number or amount of pills"

Evidence Table C-4. Results of included systematic reviews addressing harms, effectiveness and unintended effects of patient and family education or engagement related to use of prescribed or ordered opioids

Author, Year	Intervention	Outcome Category	Results
Avery, 2022[14]	Pain self-management; usually biopsychosocial or focus on improving function, with tapering	Pain intensity or distress	Moderate effect on pain intensity favoring pain self-management (standardized mean difference –0.59 (95% CI: –1.02 to –0.16), low level certainty
Avery, 2022[14]	Pain self-management; usually biopsychosocial or focus on improving function, with tapering	Total MME per prescription or per patient	Compared to no pain self-management moderately reduced opioid dose (mg OME per day) (mean difference –14.31 mg oral morphine equivalent, (95% CI: –21.57 to –7.05) based on 5 studies, moderate level certainty
Haegerich, 2019[16]	Nonpharmacological treatment and ambulatory care support sessions	Pain intensity or distress	Significant reduction in pain
Kadakia, 2020[19]	Patient educational interventions targeting opioid medications	Pain intensity or distress	No statistically significant difference in pain severity in one relevant study
Kadakia, 2020[19]	Patient educational interventions targeting opioid medications	Overdose rates	No statistically significant difference in rates of overdose events leading to medical attention or death between intervention and comparison arms, in one study.
Kadakia, 2020[19]	Patient educational interventions targeting opioid medications	Total MME per prescription or per patient	One study showed adjusted MME was not statistically significantly different
Lovecchio, 2019[22]	Counseling by anesthesiologists	Pain intensity or distress	Opioid consumption reduced by half (from historical data)
Lovecchio, 2019[22]	Physician counseling on pain management expectations	Pain intensity or distress	73% of patients in the intervention group ceased opioid use by 6 weeks (vs. 64% of the controls, p = 0.012), no difference in rates of cessation at 12 weeks or greater
Lovecchio, 2019[22]	Pre-operative patient education	Pain intensity or distress	6 weeks post-operatively, interventional group consumed fewer opioid pills (avg. 87.2 ± 98.3 vs. 51.2 ± 57.7, p < 0.01)
Lovecchio, 2019[22]	Pre-operative patient education	Pain intensity or distress	6 weeks post-operatively, interventional group had a lower average VAS pain score (3.7 ± 2.4 vs. 2.4 ± 2.0, p = 0.001)
Zhang, 2020[26]	Patient-mediated intervention (change in provider behavior through interactions with patients)	Pain intensity or distress	Patients in the intervention group experienced lower intensity and duration of pain in one study in comparison to the control
Zhang, 2020[26]	Patient-mediated intervention (change in provider behavior through interactions with patients)	Total MME per prescription or per patient	One study showed intervention reduced amount of opioids* prescribed significantly by 150 MME (95% CI: 133.5 to 166.5)
Zorrilla-Vaca, 2022[27]	Perioperative opioid education strategy	Opioid refill requests	In 4 studies, no difference in opioid refills between both groups at 15 days (OR, 0.57; 95% CI, 0.28–1.15; p =.12) and 6 weeks (OR, 1.08; 95% CI, 0.59–1.98; p =.80)

CI = confidence interval; mg = milligram; MME = morphine milligram equivalent; OME = oral morphine equivalent; OR = odds ratio

*"amount of opioids" when used in these studies means "number or amount of pills"

Evidence Table C-5. Results of included systematic reviews addressing harms, effectiveness and unintended effects of tracking, monitoring, and reporting performance data

Author, Year	Intervention	Outcome Category	Results
Liu, 2020[21]	Assessment of prescription appropriateness	Rates of opioid prescribing or ordering	One study showed no change in opioid prescribing
Liu, 2020[21]	Patient controlled analgesia safety monitoring	Overdose rates	Patient-controlled analgesia overdoses decreased in 1 study

Evidence Table C-6. Results of included systematic reviews addressing harms, effectiveness and unintended effects of clinical accountability interventions

Author, Year	Intervention	Outcome Category	Results
Raoul, 2022[24]	Clinician peer comparisons	Rates of opioid prescribing or ordering	Interrupted time series studies: reduced rate of opioid prescription at 6 months, change -28.10 (95% CI: -44.83 to -11.38) Pre-post/RCT studies: reduced rate of opioid prescription, OR 0.46 (95% CI: 0.29 to 0.72)
Raoul, 2022[24]	Clinician peer comparisons	Total MME per prescription or per patient	Pre-post/RCT studies: reduced rate of opioid prescription quantity, SMD -0.51 (95% CI: -1.10 to 0.08)

CI = confidence interval; OR = odds ratio; RCT = randomized controlled trial; SMD = standardized mean difference

Evidence Table C-7. Results of included systematic reviews addressing harms, effectiveness and unintended effects of multicomponent interventions

Author, Year	Intervention	Outcome Category	Results
Haegerich, 2019[16]	System policies such as opioid dosing limits plus education	Pain intensity or distress	No significant difference in patient pain after policy initiation
Haegerich, 2019[16]	System policies such as opioid dosing limits plus education	Rates of opioid prescribing or ordering	"Decrease in opioid prescribing" after implementation
Langford, 2023[20]	Multicomponent interventions	Pain intensity or distress	Multidisciplinary pain programs were consistently associated with reduced opioid use compared to usual care
Langford, 2023[20]	Multicomponent interventions	Pain intensity or distress	Patient-targeted interventions showed improved or unchanged pain
Langford, 2023[20]	Multicomponent clinician-focused interventions consisting of training plus decision tools	Total MME per prescription or per patient	One study reported opioid dose reduction with a significant difference
Liu, 2020[21]	Adverse event monitoring plus other interventions such as computerized order entry or drug safety guidelines	Adverse consequences	Decreased opioid-related adverse drug events (50.5 vs 31.9%). Other studies showed no change (including mortality)
Liu, 2020[21]	Adverse event monitoring plus other interventions such as computerized order entry or drug safety guidelines	Healthcare utilization (focusing on emergency department use and hospitalizations for adverse events)	No change in hospital length of stay in one hospital
Liu, 2020[21]	Adverse event monitoring plus other interventions such as computerized order entry or drug safety guidelines	Rates of opioid prescribing or ordering	Decreased opioid use
Liu, 2020[21]	Clinician education emphasizing nonopioid approaches including protocols, audit and feedback or patient involvement	Pain intensity or distress	Decrease in pain intensity among five included studies. Example: Numerical rating scale: 4.31 vs 2.94
Liu, 2020[21]	Clinician education emphasizing nonopioid approaches including protocols, audit and feedback or patient involvement	Patient satisfaction	One study reported increased patient satisfaction with pain treatment
Liu, 2020[21]	Clinician education emphasizing nonopioid approaches including protocols, audit and feedback or patient involvement	Healthcare utilization (focusing on emergency department use and hospitalizations for adverse events)	Decrease in hospital length of stay (76.6 vs 56.1 hours) and 90-day hospital admission. One study reported no change in hospital length of stay

Author, Year	Intervention	Outcome Category	Results
Liu, 2020[21]	Clinician education emphasizing nonopioid approaches, including protocols, audit and feedback or patient involvement	Rates of nonopioid analgesic prescribing	Increase in nonopioid analgesic use in 3 studies
Liu, 2020[21]	Clinician education emphasizing nonopioid approaches, including protocols, audit and feedback or patient involvement	Rates of opioid prescribing or ordering	One study showed no change in morphine use, while another study showed an increase in morphine use, and a third study showed a decrease in morphine use
Phinn, 2023[23]	Discussions with the patient about analgesia, decreasing the maximum opioid prescription quantity to 25 tablets	Rates of opioid prescribing or ordering	Decrease in the number of opioids prescribed by 20%
Phinn, 2023[23]	Modifications to the prescribing workflow or environmental remodeling in addition to prescriber education	Rates of opioid prescribing or ordering	Decrease in the number of opioids prescribed by 50-59%
Phinn, 2023[23]	Prescriber education, tools to guide opioid prescribing, reduction of the default standard prescription order, patient education, and public education	Rates of opioid prescribing or ordering	Decrease in the number of opioids prescribed per encounter by 58%

Evidence Table C-8. Results of included systematic reviews addressing harms, effectiveness and unintended effects of a combination of interventions

Author, Year	Intervention	Outcome Category	Results
Carnes, 2022[15]	Intervention that could affect the opioid prescription rate, including local/departmental interventions designed by clinicians such as guidelines for opioid prescriptions, analgesic escalation protocols, change in default electronic medical record opioid prescription (number of tablets), prescriber instructions and patient education; as well as systematic/regulatory interventions including state-mandated, legislative, and enhanced recovery after surgery protocols	Opioid refill requests	No difference in the number of patients requiring additional opioid prescriptions (RR 1.06 (95% CI 0.57 to 1.96, p<0.86)
Carnes, 2022[15]	Intervention that could affect the opioid prescription rate, including local/departmental interventions designed by clinicians such as guidelines for opioid prescriptions, analgesic escalation protocols, change in default electronic medical record opioid prescription (number of tablets), prescriber instructions and patient education; as well as systematic/regulatory interventions including state-mandated, legislative, and enhanced recovery after surgery protocols	Pain intensity or distress	No significant difference in the pain scores after receiving fewer opioid prescriptions (prescription type not specified). Meta-analysis with two studies SMD 0.16 (95% CI: -0.03 to 0.34), p=0.10
Carnes, 2022[15]	Intervention that could affect the opioid prescription rate, including local/departmental interventions designed by clinicians such as guidelines for opioid prescriptions, analgesic escalation protocols, change in default electronic medical record opioid prescription (number of tablets), prescriber instructions and patient education; as well as systematic/regulatory interventions including state-mandated, legislative, and enhanced recovery after surgery protocols	Patient satisfaction	No significant difference in pre-post cohorts regarding number of phone calls for inadequate pain control. Meta-analysis with three studies RR 1.12 (95% CI: 0.68 to 1.84)

Author, Year	Intervention	Outcome Category	Results
Carnes, 2022[15]	Intervention that could affect the opioid prescription rate, including local/departmental interventions designed by clinicians such as guidelines for opioid prescriptions, analgesic escalation protocols, change in default electronic medical record opioid prescription (number of tablets), prescriber instructions and patient education; as well as systematic/regulatory interventions including state-mandated, legislative, and enhanced recovery after surgery protocols	Patient satisfaction	No significant difference in the patient-reported satisfaction with analgesia (p=0.51) after receiving fewer opioid prescriptions. Meta-analysis from two studies SMD -0.08 (95% CI: -0.32 to 0.16)
Carnes, 2022[15]	Intervention that could affect the opioid prescription rate, including local/departmental interventions designed by clinicians such as guidelines for opioid prescriptions, analgesic escalation protocols, change in default electronic medical record opioid prescription (number of tablets), prescriber instructions and patient education; as well as systematic/regulatory interventions including state-mandated, legislative, and enhanced recovery after surgery protocols	Healthcare utilization (focusing on emergency department use and hospitalizations for adverse events)	No significant difference in pre-post cohorts regarding number of patients requiring emergency visits for pain. Meta-analysis with two studies RR 1.88 (95% CI: 0.71 to 4.95)
Carnes, 2022[15]	Intervention that could affect the opioid prescription rate, including local/departmental interventions designed by clinicians such as guidelines for opioid prescriptions, analgesic escalation protocols, change in default electronic medical record opioid prescription (number of tablets), prescriber instructions and patient education; as well as systematic/regulatory interventions including state-mandated, legislative, and enhanced recovery after surgery protocols	Rates of opioid prescribing or ordering	A significant reduction in prescribed opioids at discharge was noted in 18 out of 19 studies. The mean overall reduction in the post-intervention cohort was 67.59 MME (95% CI 54.23 to 80.94, p <0.001). For local/departmental interventions, the reduction was 76.68 MME (95% CI 60.04 to 93.31, p <0.001).

Author, Year	Intervention	Outcome Category	Results
Raoul, 2022[24]	Education, policy, and guidelines interventions	Rates of opioid prescribing or ordering	Interrupted time series studies: reduced rate of opioid prescription at 6 months, change -33.31 (95% CI: -39.67 to -26.94) Pre-post/cohort studies: reduced rate of opioid prescription, OR 0.47 (95% CI: 0.33 to 0.69)
Raoul, 2022[24]	Education, policy, and guidelines interventions	Total MME per prescription or per patient	Interrupted time series studies: reduced rate of opioid prescription quantity at 6 months, change -15.38 (95% CI: -24.51 to -6.25) Pre-post/cohort studies: reduced rate of opioid prescription quantity, SMD -0.37 (95% CI: -0.58 to -0.15)
Wong, 2020[25]	Four types of interventions (most were multicomponent): electronic medical record alerts, primary care contact and referral, individualized care plans or pathways, and departmental opioid restriction policies	Healthcare utilization (focusing on emergency department use and hospitalizations for adverse events)	A reduction in ED visits by between 48.4 and 89.5% (pre-post comparison, based on 12 studies of those included). Nine of the 10 studies that reported statistics reported a statistically significant decrease.
Wong, 2020[25]	Four types of interventions (most were multicomponent): electronic medical record alerts, primary care contact and referral, individualized care plans or pathways, and departmental opioid restriction policies	Total MME per prescription or per patient	-Reported a decrease in the total administration of opioid medications in the ED (1 out of 3 studies showing statistical significance). -All studies reported a statistically significant reduction in the number of opioid prescriptions at discharge following the implementation of their respective intervention ($p < 0.05$ to $p < 0.001$).
Avery, 2022[14]	Complementary and alternative medicine	Pain intensity or distress	Acupuncture had no effect on pain intensity standardized mean difference 0.02 (95% CI: –0.29 to 0.34), based on 3 studies, very low level certainty
Avery, 2022[14]	Complementary and alternative medicine	Total MME per prescription or per patient	Acupuncture had little or no effect on opioid dose compared to no additional acupuncture, mean difference –1.56 mg oral morphine equivalent per day (95% CI: –19.03 to 15.92), based on 3 studies, very low level certainty
Avery, 2022[14]	Pharmacological and biomedical devices and interventions	Rates of opioid prescribing or ordering	Patients receiving spinal cord stimulation were more likely to discontinue opioids than those who received conventional medical treatment, risk ratio 6.07 (95% CI: 1.16 to 31.77) based on 2 studies, very low level certainty.

CI = confidence interval; ED = emergency department; mg = milligram; MME = morphine milligram equivalent; OR = odds ratio; RR = risk ratio; SMD = standardized mean difference

Evidence Table C-9. Results of included systematic reviews addressing harms, effectiveness and unintended effects of other types of interventions

Author, Year	Intervention	Outcome Category	Results
Haegerich, 2019[16]	Community coalitions	Healthcare utilization (focusing on emergency department use and hospitalizations for adverse events)	Interventions were associated with lower ED visits, but the effect of medication assisted treatment (not specified) stabilized and rates began to increase again.
Haegerich, 2019[16]	Community coalitions	Overdose rates	Programs for patients with pain were associated with lower overdose mortality rates
Haegerich, 2019[16]	Lock-in programs within Medicaid populations	Healthcare utilization (focusing on emergency department use and hospitalizations for adverse events)	One time series study showed significant decrease in ED visits.
Haegerich, 2019[16]	Lock-in programs within Medicaid populations	Number of pills per prescription	Three time series showed significant decrease in “quantities of opioids prescribed”
Haegerich, 2019[16]	Naloxone education and distribution	Healthcare utilization (focusing on emergency department use and hospitalizations for adverse events)	One study showed decrease in opioid-related ED visits after providers and clinic staff were trained in naloxone prescribing
Haegerich, 2019[16]	Naloxone education and distribution	Overdose rates	An RCT found overdose rates did not significantly change between intervention and control participants.
Haegerich, 2019[16]	Opioid-relevant state policy (legislation/regulation)	Overdose rates	One study showed Florida's legislation saved 1029 lives in 34 months from overdosing. Another study showed similar results with a 27% decrease in overdose deaths, however there was a concurrent increase in heroin overdose death rates. It is unclear "whether this increase was due to state policy changes or due to changes in illicit drug supply”
Haegerich, 2019[16]	Opioid-relevant state policy (legislation/regulation)	Total MME per prescription or per patient	Significant decrease in opioid volume and MME.
Haegerich, 2019[16]	Prior authorization (PA) policies in the Medicaid population	Rates of opioid prescribing or ordering	Only strict PA policies were associated with a significant decrease (34%) in oxycodone use
Haegerich, 2019[16]	Public education interventions	Overdose rates	Survey respondents were less likely to share medications and take medications not prescribed to them after the campaign. Implementation was accompanied by a 14% one-year reduction in unintentional opioid-related drug overdose deaths.
Haegerich, 2019[16]	Safe storage and disposal interventions	Overdose rates	Patients were significantly less likely to practice unsafe use of prescription opioids (18% vs. 25%) compared to the control group.

Author, Year	Intervention	Outcome Category	Results
Haegerich, 2019[16]	State prescription drug monitoring programs	Overdose rates	Of 3 studies reporting on overdose rates, 2 found no significant difference or change, while one reported lower death rates with a prescription drug monitoring program compared to those without.
Haegerich, 2019[16]	State prescription drug monitoring programs	Rates of opioid prescribing or ordering	4 studies found significant decrease in prescribing.
Haegerich, 2019[16]	State prescription drug monitoring programs	Total MME per prescription or per patient	Two studies did not find a significant difference in average MME dispensed.
Liu, 2020[21]	Improving pain control	Pain intensity or distress	Two studies showed decrease in no or mild pain at rest (66.0% vs 51.0%) and activity (52.0% vs 38.0%) and (OR 2.54, 95% CI 1.22–5.65). Similarly, two studies showed no change in pain intensity
Liu, 2020[21]	Improving pain control	Patient satisfaction	Increase in patient satisfaction with pain management
Liu, 2020[21]	Improving pain control	Healthcare utilization (focusing on emergency department use and hospitalizations for adverse events)	Decreased hospital length of stay, from 5.9 to 5.1 days, No change in ICU length of stay
Liu, 2020[21]	Improving pain control	Rates of opioid prescribing or ordering	This review reported the following for opioid prescribing: One study showed no change in opioid use, while three studies showed an increase in opioid use (98.0 vs 48.0%). Increase in adherence of pethidine prescriptions to appropriateness criteria (30.0 vs 43.0%) but another study reported decrease in pethidine use. One study reported increase in morphine use
Liu, 2020[21]	Pain assessment tool	Rates of opioid prescribing or ordering	Reported under opioid prescribing: No change in opioid analgesic use
Liu, 2020[21]	Pain monitoring	Pain intensity or distress	Decreased pain incidence, intensity, with several studies showing increased pain relief
Liu, 2020[21]	Pain monitoring	Healthcare utilization (focusing on emergency department use and hospitalizations for adverse events)	No change in ICU length of stay in two studies
Liu, 2020[21]	Pain monitoring	Rates of opioid prescribing or ordering	Increase in fentanyl use, but no change in morphine use. Increase in adherence to fentanyl prescription guidelines.
Liu, 2020[21]	Prescription drug monitoring program data	Rates of opioid prescribing or ordering	Decrease in opioids prescribed in 25.1% (45 of 179) cases than initially intended, no change in number of controlled substance prescription
Raoul, 2022[24]	Any intervention mentioned in the article	Opioid refill requests	No change in need for additional opioid prescriptions

Author, Year	Intervention	Outcome Category	Results
Raoul, 2022[24]	Any intervention mentioned in the article	Patient satisfaction	1 study had a very low survey response rate (1.9%), 2 reported no impact, and 1 found a slight gain in satisfaction (from 52%to 61%).
Raoul, 2022[24]	Physical therapy consultation	Rates of opioid prescribing or ordering	Pre-post/cohort studies: reduced rate of opioid prescription, OR 0.98 (95% CI: 0.49 to 1.95)
Raoul, 2022[24]	Prescription drug monitoring program or state law	Rates of opioid prescribing or ordering	Interrupted time series studies: reduced rate of opioid prescription at 6 months, change -11.18 (95% CI: -22.34 to -0.03) Pre-post/cohort studies: reduced rate of opioid prescription, OR 0.61 (95% CI: 0.44 to 0.86)
Raoul, 2022[24]	Prescription drug monitoring program or state law	Total MME per prescription or per patient	Interrupted time series studies: reduced rate of opioid prescription quantity at 6 months, change 3.62 (95% CI: 2.39 to 4.85) Pre-post/cohort studies: reduced rate of opioid prescription quantity, SMD -0.37 (95% CI: -0.58 to -0.15)
Zhang, 2020[26]	Clinical practice guidelines: Centers for Disease Control and Prevention (CDC) opioid prescribing guidelines	Total MME per prescription or per patient	Amount of opioid* prescribed decreased by 135.2 MMEs after guideline publication (95% CI, 46.1–224.3)

CI = confidence interval; ED = emergency department; ICU = intensive care unit; MME = morphine milligram equivalent; OR = odds ratio; PA = prior authorization; RCT = randomized controlled trial

*"amount of opioids" when used in these studies means "number or amount of pills"

Evidence Table C-10. Characteristics of included primary studies addressing effects of opioid stewardship practices

Author, Year	Study Dates	Study Design	Study Setting; Single or Multiple Centers	Clinical Condition	Data Collection Methods	Fundings
Ahmed, 2016[28]	January 2013 to August 2014	Nonrandomized interventional study	Emergency Department; Single	Migraine	Surveys, electronic medical records	No funding
Bachhuber, 2021[29,30]	June 2016 to June 2018	Cluster Randomized Control Trial (CRT)	Primary care and Emergency Department; Single	Patients who (1) received a new opioid analgesic prescription at a study site, defined as no other opioid analgesic prescription of any type in the preceding 6 months (a definition used in previous cohort studies); (2) were aged 18 years or older; and (3) had no ICD-10-CM diagnosis code for cancer within 1 year before the new opioid analgesic prescription.	EHR system	National Institute on Drug Abuse, the National Center for Advancing Translational Sciences
Bachhuber, 2022[30]	June 2016 to June 2018	Cluster Randomized Control Trial (CRT)	Ambulatory Care: dental sites; Single	Patients who (1) received a new opioid analgesic prescription at a study site, defined as no other opioid analgesic prescription of any type in the preceding 6 months (a definition used in previous cohort studies); (2) were aged 18 years or older; and (3) had no ICD-10-CM diagnosis code for cancer within 1 year before the new opioid analgesic prescription.	EHR system	National Institute on Drug Abuse and the National Center for Advancing Translational Sciences
Delara, 2022[36]	January 2019 to April 2020	RCT	Ambulatory Care; Single	Minimally invasive hysterectomy	Pill count, pill diary, survey	Mayo Clinic Small Grants Program
Egan, 2020[33]	NR	RCT	Ambulatory Care; Single	Mastectomy and immediate, alloplastic breast reconstruction	EHR system, questionnaire	No funding

Author, Year	Study Dates	Study Design	Study Setting; Single or Multiple Centers	Clinical Condition	Data Collection Methods	Fundings
Kasman et al, 2021[43]	October 2017 to September 2019	Prospective Cohort	Ambulatory Care; Single	Ureteroscopy patients with urinary calculi	Review of medical records and participant prospective followup	No funding
Lamm, 2022[46]	November 2019 to July 2021	Prospective Cohort	Inpatient; Single	Inguinal hernia repair	Electronic medical record and/or by utilization of a brief telephone survey	No funding
Liebschutz, 2017[40]	January 2014 to March 2016	Cluster Randomized Control Trial (CRT)	Ambulatory Care; Multi	Adult patients treated by an enrolled primary care clinician on long-term opioid therapy (3 opioid prescriptions at least 21 days apart in a 6-month period)	EHR system	National Institute on Drug Abuse
Long, 2022[37]	June 2020 to November 2021	Prospective, randomized, open-label, noninferiority clinical trial	Ambulatory Care; Single	Patients who underwent isolated mid-urethral sling placement	Diaries, surveys, PDMP	National Institutes of Health
Martinson, 2023[47]	Not reported	Observational study with a comparison group	Ambulatory Care; Single	Long term opioid therapy	Data collected from medical records	None declared
Minegeshi, 2022[38]	April 2018 to November 2019	RCT	Ambulatory Care; Multi	Patients on opioids deemed very high risk of serious adverse events per the Stratification Tool for Opioid Risk Mitigation (STORM) dashboard	Data extracted from VHA databases	Department of Veterans Affairs
Morasco, 2022[45]	June 2016 to October 2018	Cluster Randomized Control Trial (CRT)	Ambulatory Care; Single	Patients on long-term opioid therapy	EHR data, urine drug screening results, PDMP, patient self -report surveys and measures	VA Health Services Research & Development

Author, Year	Study Dates	Study Design	Study Setting; Single or Multiple Centers	Clinical Condition	Data Collection Methods	Fundings
Neven, 2016[39]	March 2012 to July 2012	RCT	Emergency Department: Multi	Adult patients with 5 or more ED visits to study hospitals in the previous 12 months with at least half of visits attributed to pain or “drug-seeking behaviors”	Medical records, PDMP	Centers for Disease Control and Prevention
Sada, 2019[31]	November 2015 to September 2016	Quality Improvement	Ambulatory Care; Single	Mastectomies with concurrent tissue-expander placement	Data abstracted from medical records	No funding or financial support
Samet, 2021; Colasanti, 2022[41,42]	September 2015 to December 2016	Cluster Randomized Control Trial (CRT)	Ambulatory Care; Multi	People living with human immunodeficiency virus (PLWH) on chronic opioid therapy (COT)	Web based registry, questionnaires	National Institute on Drug Abuse, Emory Center for AIDS Research, and the Boston/Providence Center for AIDS Research
Stepan, 2021[35]	May 2017 to April 2019	RCT	Ambulatory Care; Single	Patients scheduled to undergo outpatient elective "nonminor" hand surgery	Postoperative log and surveys	American Foundation for Surgery of the Hand and the Hospital for Special Surgery
Syed, 2018[32]	August 2015 to December 2016	RCT	Ambulatory Care; Single	Patients undergoing primary arthroscopic rotator cuff repair	EHR system, questionnaire	NR
Vitzthum, 2022[44]	2011 to 2016	Observational study with a comparison group	Ambulatory Care; Multi	Cancer treatment	Data collected from Veterans Health Affairs’ database and cancer registry database, and ICD 9 and 10 codes	ASCO Conquer Cancer Foundation Young Investigator, VA Career Development Award, and National Institute on Drug Abuse of the National Institutes of Health

Author, Year	Study Dates	Study Design	Study Setting; Single or Multiple Centers	Clinical Condition	Data Collection Methods	Fundings
Voepel-Lewis, 2021[34]	NR	RCT	Ambulatory or short-stay hospitalization; Single	"Children, aged 5 to 17 years, [who] were scheduled to undergo ambulatory or short-stay surgery and expected to receive an opioid prescription to manage postoperative pain."	Semi structured diaries and surveys	National Institute on Drug Addiction

AIDS = acquired immunodeficiency syndrome; ASCO = American Society of Clinical Oncology; EHR = electronic health record; ICD = International Classification Code; ICD-10-CM = International Statistical Classification of Diseases, 10th Revision, Clinical Modification; NR = not reported; PDMP = prescription drug monitoring program; RCT = randomized controlled trial; VA = Veteran Affairs; VHA = Veteran Health Administration

Evidence Table C-11. Intervention characteristics of primary studies addressing effects of opioid stewardship practices

Author, Year	Comparator	Intervention Category	Intervention Description
Ahmed, 2016[28]	Control – pre-intervention	Multicomponent	Acute headache management algorithm was implemented in the Lakewood Hospital ED, a small regional Cleveland Clinic affiliated hospital in Lakewood, OH. The algorithm was posted online as well as available in a hardcopy format alongside other commonly used protocols. The first step of the algorithm directs ED staff to use the Sheftell and Cady three question headache screening tool to diagnose migraine. A migraine diagnosis prompts the ED provider to screen for comorbid psychiatric or substance abuse disorders.
Bachhuber, 2021[29]	Control - usual EHR	Clinical decision support or electronic health record interventions	Site level change to the electronic health record to implement a uniform, reduced, default dispense quantity of 10 tablets for new opioid analgesics prescriptions
Bachhuber, 2022[30]	Control - usual EHR	Clinical decision support or electronic health record interventions	Site-level change to the EHR to implement a uniform, reduced, default dispense quantity of 10 tablets or 5 tablets for new opioid analgesic prescriptions.
Delara, 2022[36]	Standard prescription of 30 tablets of oxycodone 5 mg, ibuprofen 600 mg every 6 hours, and acetaminophen 1000 mg every 6 hours with no education/engagement. Emphasized use of nonopioid analgesia and reviewed potential side effects of opioids per standard practice.	Patient and family education or engagement related to use of prescribed or ordered opioids	For the patient-directed arm, a shared decision-making framework was provided by trained research staff. A written script guided the research staff to initiate conversation with the patient, describing the reason for opioid prescribing, common side effects and risks of taking opioids, and recommended management of pain. Using this framework, patients were provided the opportunity to give insight into the number of opioid tablets that they felt were appropriate for their post-operative management, which was then prescribed by the research team
Egan, 2020[33]	Control - Standard patient counseling from the surgical and perioperative teams	Patient and family education or engagement related to use of prescribed or ordered opioids	Standard of care plus an educational instrument containing information about pain expectations and goals, examples of opioid and adjunct medications which may be used perioperatively, risks associated with opioid use and examples of non-medication pain control methods and statements to normalize the pain experience for the patient
Kasman et al, 2021[43]	Control – historical controls	Multicomponent	The opioid-free protocol at discharge involved interventions at 5 distinct steps: 1) preoperative clinic visit, 2) preoperative surgical staging area, 3) intraoperative, 4) postanesthetic care unit (PACU), and 5) discharge

Author, Year	Comparator	Intervention Category	Intervention Description
Lamm, 2022[46]	Control – no intervention	Multicomponent	The protocol included: a) an educational component provided at the outpatient visit with the surgeon with instructions tailored to the specific procedure, as well as the ACS Safe and Effective Pain Control After Surgery patient tool; b) preoperative multimodal analgesia provided 1 hour prior to operation; c) goal-directed fluid management, limited intraoperative opioid administration at the discretion of the anesthesiologist, and local anesthetic administered at incision sites; d) postoperative elements of the protocol included limited post-anesthesia care unit administration of opioids based on pain scores (opioids only allowed for pain visual analog score > 6), discharge counseling regarding limited opioid use at home, and instructions to alternate between acetaminophen and ibuprofen every 3 hours at home for pain.
Liebschutz, 2017[40]	Control - electronic decision tools alone	Multicomponent	TOPCARE intervention (nurse care management, electronic registry, academic detailing, and electronic decision tools)
Long, 2022[37]	Control - standard prescription of ten oxycodone 5 mg tablets provided preoperatively	Patient and family education or engagement related to use of prescribed or ordered opioids	Receive a prescription of ten oxycodone 5 mg tablets postoperatively, only upon patient request
Martinson, 2023[47]	Control – PC-POP non-enrollees	Multicomponent	PC-POP is made up of an interdisciplinary care management consult team that implements the VA/DoD recommended guidelines for LOT among patients with chronic pain being managed in primary care. During the study timeframe, PC-POP was staffed by two certified nurse practitioners, a psychologist, and four registered nurses. Patients enrolled in the program attend a shared medical appointment every 6 months or until discontinuation of opioid therapy.
Minegeshi, 2022[38]	Non-oversight - A policy notice specifying that at least 97% of patients displayed as very high risk on the STORM dashboard be case-reviewed if they have not been in the past 12 months.	Other	An extra paragraph of the policy notice stating that facilities not meeting the target will receive technical assistance and be required to submit an action plan focused on improving the case review rate

Author, Year	Comparator	Intervention Category	Intervention Description
Morasco, 2022[45]	Education Only: a two-hour educational session for clinicians on patient-centered care surrounding prescription opioid adherence monitoring. Encouraged to provide usual care as indicated	Multicomponent	Two-hour educational session for clinicians on patient-centered care surrounding prescription opioid adherence monitoring. In addition, the improving the safety of opioid therapy (ISOT) initiative consisted of a nurse care manager, internal medicine physician with expertise in chronic pain treatment in primary care and psychologist with expertise in treating comorbid pain and substance use disorder. The nurse manager reviewed records and met with patients to provide rationale for screenings and education and tailored recommendations to PCP about improving opioid safety. Included a registry and nurse manager could consult with the physician and psychologist to provide support.
Neven, 2016[39]	Control - treatment as usual	Multicomponent	Case manager to assist with barriers to care, multidisciplinary discussion of patients to develop individualized ED plans documented in the ED information exchange system that faxed the guideline to the treating provider when the patient presents to the ED.
Sada, 2019[31]	Prior guideline phases	Multicomponent	Guidelines for post discharge prescriptions were developed. During phase I, 16 patients were surveyed to determine baseline prescribed MMEs and rate of satisfaction. A guideline was subsequently developed to standardize post discharge prescribing (550 MMEs prescribed for patients with average risk of pain vs 900 MMEs fopr patients with high risk of pain). The survey was repeated in phase II.

Author, Year	Comparator	Intervention Category	Intervention Description
Samet et al., 2021; Colasanti, 2022[41,42]	Control - an informational brochure summarizing guidelines for chronic opioid therapy and listing a web resource with electronic tools	Multicomponent	The 12-month Targeting Effective Analgesia in Clinics for HIV (TEACH) intervention consisted of 3 components: (1) a nurse care manager with an interactive electronic registry to manage patients; (2) opioid education and academic detailing; and (3) facilitated access to addiction specialists. Each site hired a nurse care manager (NCM) with a background in HIV care and interest in addiction. Intervention providers received a 60-minute group didactic session from a study investigator expert on opioid prescribing; Providers participated in two 30-minute individual academic detailing sessions 2–3 months apart throughout the year-long intervention with an option of a third. The NCM utilized a HIPAA (Health Insurance Portability and Accountability Act)–compliant, web-based registry specifically built using user-based design methods to record and generate individual or aggregate information in real-time reports on opioid treatment agreements, UDTs, pill counts and checking prescription monitoring programs
Stepan, 2021[35]	Control - Routine perioperative counseling surrounding surgery and pain management according to individual surgeon's standard of care	Patient and family education or engagement related to use of prescribed or ordered opioids	Standard of care education and postoperative instructions plus 7 minutes of education on postoperative pain management via video along with a laminated card with a summary of the preoperative pain education as part of postoperative instructions
Syed, 2018[32]	Control - normal preoperative education regarding surgery	Patient and family education or engagement related to use of prescribed or ordered opioids	Formal education detailing recommended postoperative opioid usage, side effects, dependence, and addiction via a 2-minute narrated video and a handout detailing the risks of narcotic overuse and abuse
Vitzthum, 2022[44]	Pre-intervention	Dashboards	Opioid Sparing Initiative: A program dashboard aggregated patient-, clinician-, and facility-level data on opioid prescribing, including high-risk prescriptions such as high daily opioid doses (defined as 100 MME) and concomitant benzodiazepine prescriptions. To guide safer prescribing, providers were alerted to prescribing patterns identified as high risk opioid prescribing or deviated from the institutional standard of care.

Author, Year	Comparator	Intervention Category	Intervention Description
Voepel-Lewis, 2021[34]	Control - Routine instruction including a standardized, computer-generated discharge instruction sheet that included prescription information and listed common postoperative adverse effects with instructions to call the clinic if unmanageable	Patient and family education or engagement related to use of prescribed or ordered opioids	Routine instruction plus the Scenario-Tailored Opioid Messaging Program [STOMP] educational intervention, designed to provide scenario-specific opioid risk and benefit information meant to promote better decisions toward pain and ADE reduction.

ACS = American College of Surgeons; ADE = adverse drug effects; DoD = Department of Defense; ED = emergency department; EHR = electronic health record; HIPAA = Health Insurance Portability and Accountability Act; HIV = human immunodeficiency virus; LOT = long-term opioid therapy; mg = milligram; MME = morphine milligram equivalent; NCM = nurse care manager; PC-POP = Primary Care Pain Education and Opioid Monitoring Program; STORM = Stratification Tool for Opioid Risk Mitigation; TOPCARE = Transforming Opioid Prescribing in Primary Care; UDT = urine drug tests; VA = Veteran Affairs

Evidence Table C-12. Patient characteristics of primary studies addressing effects of opioid stewardship practices

Author, Year	Arm	Arm Name	N at Baseline	Gender, n (%)	Age	Race, n (%)
Ahmed, 2016[28]	Arm 1	Pre-protocol	50	Female: 44 (88) Male: NR	Mean: 39.6 (SD 14)	NR
Ahmed, 2016[28]	Arm 2	Post-protocol (cohort 1 + cohort 2)	94	Female: 84 (89) Male: NR	Mean: 37.5 (SD 14)	NR
Bachhuber, 2022[29]	Arm 1	Control (Before Intervention)	3957	Female: 2571 (65) Male: NR	Median: 50.5	White: 1332 (33.7) Black or African American: 1636 (41.3) Other: 439 (11.1)
Bachhuber, 2022[29]	Arm 2	Intervention (Before Intervention)	3560	Female: 2203 (61.9) Male: NR	Median: 51.9	White: 1090 (30.6) Black or African American: 1678 (47.1) Other: 192 (5.4)
Bachhuber, 2022[29]	Arm 1	Control (After Intervention)	7651	Female: 4848 (63.4) Male: NR	Median: 50.4	White: 2460 (32.2) Black or African American: 3314 (43.3) Other: 806 (10.5)
Bachhuber, 2022[29]	Arm 2	Intervention (After Intervention)	6163	Female: 3761 (61) Male: NR	Median: 51.9	White: 1819 (29.5) Black or African American: 3044 (49.4) Other: 344 (5.6)
Bachhuber, 2022[30]	Arm 1	Control - Provider	19	Female: 6 (32) Male: NR	NR	NR
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site - Provider	17	Female: 4 (24) Male: NR	NR	NR
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site - Provider	14	Female: 0 (0) Male: NR	NR	NR
Bachhuber, 2022[30]	Arm 1	Control - Patient (Before Intervention)	522	Female: 324 (62.1) Male: NR	Median: 30.7	White: 176 (33.7) Black or African American: 166 (31.8) Other: 24 (4.6)
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site - Patient (Before Intervention)	765	Female: 461 (60.3) Male: NR	Median: 57.1	White: 75 (9.8) Black or African American: 104 (13.6) Other: 180 (23.5)

Author, Year	Arm	Arm Name	N at Baseline	Gender, n (%)	Age	Race, n (%)
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site - Patient (Before Intervention)	464	Female: 272 (58.6) Male: NR	Median: 31.8	White: 120 (25.9) Black or African American: 131 (28.2) Other: 54 (11.6)
Bachhuber, 2022[30]	Arm 1	Control - Patient (After Intervention)	1327	Female: 788 (59.4) Male: NR	Median: 32.3	White: 447 (33.7) Black or African American: 424 (32) Other: 76 (5.7)
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site - Patient (After Intervention)	2010	Female: 1151 (57.3) Male: NR	Median: 56	White: 221 (11) Black or African American: 257 (12.8) Other: 476 (23.7)
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site - Patient (After Intervention)	1221	Female: 721 (59.1) Male: NR	Median: 32.4	White: 321 (26.3) Black or African American: 391 (32) Other: 136 (11.1)
Delara, 2022[36]	Arm 1	Standard	32	Female: 32(100) Male: NR	Median: 59.5	White: 28(87.5) Black or African American: 0(0) Other: 1(3.1)
Delara, 2022[36]	Arm 2	Patient-Directed	33	Female: 33(100) Male: NR	Median: 52	White: 29(87.9) Black or African American: 2(6.1) Other: 1(3)
Egan, 2020[33]	Arm 1	Control	50	NR	Mean: 48.5 (SD 12.4)	White: 42 (84) Black or African American: 5 (10) Other: 3 (6)
Egan, 2020[33]	Arm 2	Intervention	50	NR	Mean: 51.4 (SD 11.1)	White: 40 (80) Black or African American: 7 (14) Other: 3 (6)
Kasman et al, 2021[43]	Arm 1	Control	54	Female: NR (63) Male: NR	Mean: 61 (SD NR)	NR
Kasman et al, 2021[43]	Arm 2	Intervention	54	Female: NR (46) Male: NR	Mean: 56 (SD NR)	NR

Author, Year	Arm	Arm Name	N at Baseline	Gender, n (%)	Age	Race, n (%)
Lamm, 2022[46]	Arm 1	Control	58	Female: 19 (32.8) Male: NR	Mean: 52.4 (SD 1.8)	White: 3 (5.3) Black or African American: 47 (81) Other: 1 (1.7)
Lamm, 2022[46]	Arm 2	Opioid Sparing	42	Female: 10 (23.8) Male: NR	Mean: 55.3 (SD 2)	White: 5 (11.9) Black or African American: 31 (73.8) Other: 1 (2.4)
Lamm, 2022[46]	Arm 3	No Opioid	29	Female: 2 (6.9) Male: NR	Mean: 58.6 (SD 2.9)	White: 7 (24.1) Black or African American: 22 (75.9) Other: 0 (0)
Liebschutz, 2017[40]	Arm 1	Control	399	Female: 179 (44.9) Male: NR	Mean: 55.25 (SD 11.47)	White: 207 (51.9) Black or African American: 142 (35.6) Other: 40 (10)
Liebschutz, 2017[40]	Arm 2	Intervention	586	Female: 287 (49) Male: NR	Mean: 54.4 (SD 11.51)	White: 305 (52.1) Black or African American: 219 (37.4) Other: 51 (8.7)
Liebschutz, 2017[40]	Overall	Overall	985	Female: 466 (47.3) Male: NR	Mean: 54.7 (SD 11.5)	White: 512 (52) Black or African American: 361 (36.7) Other: 91 (9.2)
Long, 2022[37]	Arm 1	Standard	40	NR	Mean: 55(SD 11.9)	White: 36(90)
Long, 2022[37]	Arm 2	Restricted	42	NR	Mean: 51.2(SD 11.8)	White: 38(92.7)
Long, 2022[37]	Overall	Overall	82	NR	Mean: 53.1(SD 11.9)	White: 74(91.4)
Martinson, 2023[47]	Arm 1	PC-POP enrollees	423	Female: NR Male: 388 (91.51)	NR	White: 401 (94.58)
Martinson, 2023[47]	Arm 2	PC-POP non-enrollees	NR	Female: NR Male: 310 (95.68)	NR	White: 310 (95.38)
Minegeshi, 2022[38]	Arm 1	Non-oversight	7538	Female: NR Male: NR (87.86)	Mean: 56.37(SD 12.87)	White: NR (67.6) Black or African American: NR (26.88) Other: NR (5.52)

Author, Year	Arm	Arm Name	N at Baseline	Gender, n (%)	Age	Race, n (%)
Minegeshi, 2022[38]	Arm 2	Oversight	8734	Female: NR Male: NR (87.57)	Mean: 55.66(SD 12.72)	White: NR (63.99) Black or African American: NR (30.97) Other: NR (5.04)
Morasco, 2022[45]	Arm 1	Education Only (Patient)	136	Female: NR Male: 115 (84.6)	Mean: 60.4 (SD 11.8)	White: 108 (79.4)
Morasco, 2022[45]	Arm 2	ISOT (Patient)	150	Female: NR Male: 135 (90)	Mean: 61.2 (SD 0.9)	White: 123 (82)
Morasco, 2022[45]	Arm 1	Education Only (Provider)	16	Female: NR Male: 5 (31.3)	Mean: 53.6 (SD 10.5)	White: 13 (81.3)
Morasco, 2022[45]	Arm 2	ISOT (Provider)	19	Female: NR Male: 10 (52.6)	Mean: 50.3 (SD 10)	White: 13 (68.4)
Neven, 2016[39]	Arm 1	Control	76	Female: 52 (72.15) Male: NR	Mean: 37.12 (SD 12.9)	NR
Neven, 2016[39]	Arm 2	Intervention	79	Female: 57 (68.42) Male: NR	Mean: 37.82 (SD 13.37)	NR
Sada, 2019[31]	Arm 1	Phase 1	16	NR	NR	NR
Sada, 2019[31]	Arm 2	Phase 2	23	NR	NR	NR
Sada, 2019[31]	Arm 3	Phase 3	22	NR	NR	NR
Sada, 2019[31]	Arm 4	Phase 4	27	NR	NR	NR
Samet, 2021; Colasanti, 2022[41,42]	Arm 1	Control (Provider)	20	Female: 14(70) Male: NR	Mean: 46.1(SD 11.7)	White: 14(70) Black or African American: 2(10) Other: 3(15)
Samet, 2021; Colasanti, 2023[41,42]	Arm 2	Intervention (Provider)	21	Female: 12(57.1) Male: NR	Mean: 45(SD 11.5)	White: 12(57.1) Black or African American: 2(9.5) Other: 4(19)
Samet, 2021; Colasanti, 2024[41,42]	Overall	Overall (Provider)	41	Female: 26(63.4) Male: NR	Mean: 45.5(SD 11.5)	White: 26(63.4) Black or African American: 4(9.8) Other: 7(17.1)
Samet, 2021; Colasanti, 2025[41,42]	Arm 1	Control (Patient)	56	Female: 18(32.1) Male: NR	Mean: 52.5(SD 8.5)	White: 11(19.6) Black or African American: 43(76.8) Other: 2(3.6)

Author, Year	Arm	Arm Name	N at Baseline	Gender, n (%)	Age	Race, n (%)
Samet, 2021; Colasanti, 2026[41,42]	Arm 2	Intervention (Patient)	58	Female: 20(34.5) Male: NR	Mean: 54.1(SD 8)	White: 15(25.9) Black or African American: 40(69) Other: 3(5.2)
Stepan, 2021[35]	Arm 1	Control	98	Female: 46(46.9) Male: 52(53.1)	Mean: 62.5(SD NR) Range: 22-84	NR
Stepan, 2021[35]	Arm 2	Education Group	93	Female: 41(44.1) Male: 52(55.9)	Mean: 58(SD NR) Range: 19-82	NR
Stepan, 2021[35]	Overall	Total	191	Female: 87(45.5) Male: 104(54.5)	Mean: 60(SD NR) Range: 19-84	NR
Syed, 2018[32]	Arm 1	Control	66	Female: NR Male: NR (68.2)	Mean: 58 (SD 9.4) Range: NR	NR
Syed, 2018[32]	Arm 2	Study	68	Female: NR Male: NR (67.6)	Mean: 59.2 (SD 9.2) Range: NR	NR
Vitzthum, 2022[44]	Arm 1	Pre-OSI	19382	Female: 979 (5) Male: 18408 (95)	Mean: 66.93 (SD 8.07)	NR
Vitzthum, 2022[44]	Arm 2	Post-OSI	22682	Female: 968 (4.3) Male: 21717 (95.7)	Mean: 66 (SD 8.21)	NR
Voepel-Lewis, 2021[34]	Arm 1	Control [Parent]	308	Female: 241(78.2) Male: NR	NR	White: 257(83.4) Black or African American: 22(7.1) Other: 11(3.6)
Voepel-Lewis, 2021[34]	Arm 2	STOMP [Parent]	296	Female: 250(84.5) Male: NR	NR	White: 254(85.8) Black or African American: 21(7.1) Other: 10(3.4)
Voepel-Lewis, 2021[34]	Arm 1	Control [Child]	308	Female: 143(46.4) Male: NR	Mean: 12.81(SD 3.68)	NR
Voepel-Lewis, 2021[34]	Arm 2	STOMP [Child]	296	Female: 115(38.9) Male: NR	Mean: 13.19(SD 3.59)	NR

ISOT = improving the safety of opioid therapy; N = sample size; NR = not reported; OSI = Opioid Safety Initiative; PC-POP = Primary Care Pain Education and Opioid Monitoring Program; Pop = population; SD = standard deviation; STOMP = Scenario-Tailored Opioid Messaging Program

Evidence Table C-13. Healthcare utilization outcome (categorical data) of primary studies addressing effects of organizational leadership and policies within a healthcare facility or healthcare system

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Outcome Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Ahmed, 2016[28]	Arm 1	Pre-protocol	Number of admissions	NR	50	4 (NR)	NR	Comparator: Arm 2 and 3 p-value only: p = 0.83	No
Ahmed, 2016[28]	Arm 2	Post-protocol (cohort 1)	Number of admissions	NR	44	3 (NR)	NR	Comparator: Arm 1 and 3 p-value only: p = 0.83	No
Ahmed, 2016[28]	Arm 3	Post-protocol (cohort 2)	Number of admissions	NR	50	17 (NR)	NR	Comparator: Arm 1 and 2 p-value only: p = 0.001	No
Ahmed, 2016[28]	Arm 1	Pre-protocol	Number with followup appointment	NR	50	27 (NR)	NR	Comparator: Arm 2 and 3 p-value only: p <0.001	No
Ahmed, 2016[28]	Arm 2	Post-protocol (cohort 1)	Number with followup appointment	NR	44	40 (NR)	NR	Comparator: Arm 1 and 3 p-value only: p <0.001	No
Ahmed, 2016[28]	Arm 3	Post-protocol (cohort 2)	Number with followup appointment	NR	50	11 (NR)	NR	Comparator: Arm 1 and 2 p-value only: p = 0.018	No
Bachhuber, 2021[29]	Arm 1	Control	Emergency department visit (Pre-Intervention)	30 days	3957	107 (2.7)	NR	NR	No
Bachhuber, 2021[29]	Arm 2	Intervention	Emergency department visit (Pre-Intervention)	30 days	3560	97 (2.7)	NR	NR	No

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Outcome Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Bachhuber, 2021[29]	Arm 1	Control	Emergency department visit (Post-Intervention)	30 days	7651	153 (2)	NR	NR	No
Bachhuber, 2021[29]	Arm 2	Intervention	Emergency department visit (Post-Intervention)	30 days	6163	127 (2.1)	NR	NR	No
Bachhuber, 2021[29]	Arm 1	Control	Emergency department visit	30 days	11608	NR	NR	Ref	No
Bachhuber, 2021[29]	Arm 2	Intervention	Emergency department visit	30 days	9723	NR	NR	Comparator: Arm 1 Difference in difference (percentage points): 0.1 (95% CI: -0.2 to 0.4), p = 0.47	No
Bachhuber, 2021[29]	Arm 1	Control	Hospitalization (Pre-Intervention)	30 days	3957	54 (1.4)	NR	NR	No
Bachhuber, 2021[29]	Arm 2	Intervention	Hospitalization (Pre-Intervention)	30 days	3560	36 (1)	NR	NR	No
Bachhuber, 2021[29]	Arm 1	Control	Hospitalization (Post-Intervention)	30 days	7651	98 (1.3)	NR	NR	No
Bachhuber, 2021[29]	Arm 2	Intervention	Hospitalization (Post-Intervention)	30 days	6163	67 (1.1)	NR	NR	No
Bachhuber, 2021[29]	Arm 1	Control	Hospitalization	30 days	11608	NR	NR	Ref	No

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Outcome Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Bachhuber, 2021[29]	Arm 2	Intervention	Hospitalization	30 days	9723	NR	NR	Comparator: Arm 1 Difference in difference (percentage points): 0.2 (95% CI: -0.08 to 0.4), p = 0.18	No
Bachhuber, 2021[29]	Arm 1	Control	Opioid analgesic prescription reorder	30 days	11608	NR	NR	Ref	No
Bachhuber, 2021[29]	Arm 2	Intervention	Opioid analgesic prescription reorder	30 days	9723	NR	NR	Comparator: Arm 1 Difference in difference (percentage points): 0.5 (95% CI: -0.7 to 1.8), p = 0.4	No
Bachhuber, 2022[30]	Arm 1	Control	Outpatient visit during the 30-day period after the index prescription (Before Intervention)	30 days	522	47 (9)	NR	NR	No

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Outcome Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site	Outpatient visit during the 30-day period after the index prescription (Before Intervention)	30 days	765	44 (5.8)	NR	NR	No
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site	Outpatient visit during the 30-day period after the index prescription (Before Intervention)	30 days	464	35 (7.5)	NR	NR	No
Bachhuber, 2022[30]	Arm 1	Control	Outpatient visit during the 30-day period after the index prescription (After Intervention)	30 days	522	86 (6.5)	NR	NR	No
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site	Outpatient visit during the 30-day period after the index prescription (After Intervention)	30 days	765	133 (6.6)	NR	NR	No

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Outcome Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site	Outpatient visit during the 30-day period after the index prescription (After Intervention)	30 days	464	84 (6.9)	NR	NR	No
Bachhuber, 2022[30]	Arm 1	Control	Outpatient visit during the 30-day period after the index prescription	30 days	1849	NR	NR	Ref	No
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site	Outpatient visit during the 30-day period after the index prescription	30 days	2775	NR	NR	Comparator: Arm 1 Difference in difference (percentage points): 3.4 (95% CI: -0.2 to 7), p = 0.08	No
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site	Outpatient visit during the 30-day period after the index prescription	30 days	1685	NR	NR	Comparator: Arm 1 Difference in difference (percentage points): 1.7 (95% CI: -0.7 to 4.2), p = 0.16	No

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Outcome Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Bachhuber, 2022[30]	Arm 1	Control	Emergency department visit during the 30-day period after the index prescription (Before Intervention)	30 days	522	4 (0.8)	NR	NR	No
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site	Emergency department visit during the 30-day period after the index prescription (Before Intervention)	30 days	765	0 (0)	NR	NR	No
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site	Emergency department visit during the 30-day period after the index prescription (Before Intervention)	30 days	464	1 (0.2)	NR	NR	No
Bachhuber, 2022[30]	Arm 1	Control	Emergency department visit during the 30-day period after the index prescription (After Intervention)	30 days	522	4 (0.2)	NR	NR	No

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Outcome Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site	Emergency department visit during the 30-day period after the index prescription (After Intervention)	30 days	765	0 (0.05)	NR	NR	No
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site	Emergency department visit during the 30-day period after the index prescription (After Intervention)	30 days	464	4 (0.3)	NR	NR	No
Bachhuber, 2022[30]	Arm 1	Control	Emergency department visit during the 30-day period after the index prescription	30 days	1849	NR	NR	Ref	No
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site	Emergency department visit during the 30-day period after the index prescription	30 days	2775	NR	NR	Comparator: Arm 1 Difference in difference (percentage points): 0.6 (95% CI: -0.2 to 1.4), p = 0.16	No

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Outcome Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site	Emergency department visit during the 30-day period after the index prescription	30 days	1685	NR	NR	Comparator: Arm 1 Difference in difference (percentage points): 0.7 (95% CI: -0.3 to 10.6), p = 0.26	No
Bachhuber, 2022[30]	Arm 1	Control	Hospitalization during the 30-day period after the index prescription (Before Intervention)	30 days	522	2 (0.4)	NR	NR	No
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site	Hospitalization during the 30-day period after the index prescription (Before Intervention)	30 days	765	0 (0)	NR	NR	No
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site	Hospitalization during the 30-day period after the index prescription (Before Intervention)	30 days	464	0 (0)	NR	NR	No

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Outcome Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Bachhuber, 2022[30]	Arm 1	Control	Hospitalization during the 30-day period after the index prescription (After Intervention)	30 days	522	4 (0.3)	NR	NR	No
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site	Hospitalization during the 30-day period after the index prescription (After Intervention)	30 days	765	0 (0)	NR	NR	No
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site	Hospitalization during the 30-day period after the index prescription (After Intervention)	30 days	464	4 (0.3)	NR	NR	No
Bachhuber, 2022[30]	Arm 1	Control	Hospitalization during the 30-day period after the index prescription	30 days	1849	NR	NR	Ref	No

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Outcome Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site	Hospitalization during the 30-day period after the index prescription	30 days	2775	NR	NR	Comparator: Arm 1 Difference in difference (percentage points): 0.1 (95% CI: -0.8 to 0.9), p = 0.84	No
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site	Hospitalization during the 30-day period after the index prescription	30 days	1685	NR	NR	Comparator: Arm 1 Difference in difference (percentage points): 0.4 (95% CI: -0.5 to 1.3), p = 0.64	No

CI = confidence interval; N = sample size; NR = not reported, Ref = reference arm

Evidence Table C-14. Opioid refill request (categorical data) of primary studies addressing effects of organizational leadership and policies within a healthcare facility or healthcare system

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Bachhuber, 2021[29]	Arm 1	Control	Opioid analgesic prescription reorder (Pre-Intervention)	30 days	3957	501 (12.7)	NR	NR	No
Bachhuber, 2021[29]	Arm 2	Intervention	Opioid analgesic prescription reorder (Pre-Intervention)	30 days	3560	424 (11.9)	NR	NR	No
Bachhuber, 2021[29]	Arm 1	Control	Opioid analgesic prescription reorder (Post-Intervention)	30 days	7651	938 (12.3)	NR	NR	No
Bachhuber, 2021[29]	Arm 2	Intervention	Opioid analgesic prescription reorder (Post-Intervention)	30 days	6163	750 (12.2)	NR	NR	No
Bachhuber, 2022[30]	Arm 1	Control	Opioid analgesic prescription reorder during the 30-day period after the index prescription (Before Intervention)	30 days	522	51 (9.8)	NR	NR	No

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site	Opioid analgesic prescription reorder during the 30-day period after the index prescription (Before Intervention)	30 days	765	50 (6.5)	NR	NR	No
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site	Opioid analgesic prescription reorder during the 30-day period after the index prescription (Before Intervention)	30 days	464	36 (7.8)	NR	NR	No
Bachhuber, 2022[30]	Arm 1	Control	Opioid analgesic prescription reorder during the 30-day period after the index prescription (After Intervention)	30 days	522	90 (6.8)	NR	NR	No
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site	Opioid analgesic prescription reorder during the 30-day period after the index prescription (After Intervention)	30 days	765	138 (6.9)	NR	NR	No

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site	Opioid analgesic prescription reorder during the 30-day period after the index prescription (After Intervention)	30 days	464	91 (7.5)	NR	NR	No
Bachhuber, 2022[30]	Arm 1	Control	Opioid analgesic prescription reorder during the 30-day period after the index prescription	30 days	1849	NR	NR	Ref	No
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site	Opioid analgesic prescription reorder during the 30-day period after the index prescription	30 days	2775	NR	NR	Comparator: Arm 1 Difference in difference (percentage points): 3.3 (95% CI: 0.2 to 6.4), p = 0.04	No
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site	Opioid analgesic prescription reorder during the 30-day period after the index prescription	30 days	1685	NR	NR	Comparator: Arm 1 Difference in difference (percentage points): 2.6 (95% CI: 0.2 to 4.9), p = 0.03	No

CI = confidence interval; N = sample size; NR = not reported

Evidence Table C-15. Rates of opioid prescribing (categorical data) of studies addressing harms, effectiveness and unintended effects of organizational leadership and policies within a healthcare facility or healthcare system

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Outcome events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Ahmed, 2016[28]	Arm 1	Pre-protocol	Number of patients treated with opioid or barbiturate	NR	50	33 (NR)	NR	Comparator: Arm 2 and 3 p-value only: p <0.001	No
Ahmed, 2016[28]	Arm 2	Post-protocol (cohort 1)	Number of patients treated with opioid or barbiturate	NR	44	3 (NR)	NR	Comparator: Arm 1 and 3 p-value only: p <0.001	No
Ahmed, 2016[28]	Arm 3	Post-protocol (cohort 2)	Number of patients treated with opioid or barbiturate	NR	50	14 (NR)	NR	Comparator: Arm 1 and 2 p-value only: p <0.001	No
Ahmed, 2016[28]	Arm 1	Pre-protocol	Number of patients discharged with opioid or barbiturate	NR	50	17 (NR)	NR	Comparator: Arm 2 and 3 p-value only: p = 0.008	No
Ahmed, 2016[28]	Arm 2	Post-protocol (cohort 1)	Number of patients discharged with opioid or barbiturate	NR	44	5 (NR)	NR	Comparator: Arm 1 and 3 p-value only: p = 0.008	No
Ahmed, 2016[28]	Arm 3	Post-protocol (cohort 2)	Number of patients discharged with opioid or barbiturate	NR	50	2 (NR)	NR	Comparator: Arm 1 and 2 p-value only: p = 0.002	No
Bachhuber, 2021[29]	Arm 1	Control	Dispense quantity 10 tablets or less (Pre-Intervention)	NR	3957	1122 (28.4)	NR	NR	No

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Outcome events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Bachhuber, 2021[29]	Arm 2	Intervention	Dispense quantity 10 tablets or less (Pre-Intervention)	NR	3560	1364 (38.3)	NR	NR	No
Bachhuber, 2021[29]	Arm 1	Control	Dispense quantity 10 tablets or less (Post-Intervention)	NR	7651	2751 (36)	NR	NR	No
Bachhuber, 2021[29]	Arm 2	Intervention	Dispense quantity 10 tablets or less (Post-Intervention)	NR	6163	3337 (54.1)	NR	NR	No
Bachhuber, 2021[29]	Arm 1	Control	Dispense quantity 10 tablets or less	NR	11608	NR	NR	Ref	No
Bachhuber, 2021[29]	Arm 2	Intervention	Dispense quantity 10 tablets or less	NR	9723	NR	NR	Comparator: Arm 1 Difference in difference (percentage points): 7.6 (95% CI: 6.1 to 9.2), p <0.001	No
Bachhuber, 2022[30]	Arm 1	Control	Dispense quantity 10 tablets or less (Before Intervention)	NR	522	120 (23)	NR	NR	No
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site	Dispense quantity 10 tablets or less (Before Intervention)	NR	765	74 (9.7)	NR	NR	No

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Outcome events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site	Dispense quantity 10 tablets or less (Before Intervention)	NR	464	63 (13.6)	NR	NR	No
Bachhuber, 2022[30]	Arm 1	Control	Dispense quantity 10 tablets or less (After Intervention)	NR	522	548 (41.3)	NR	NR	No
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site	Dispense quantity 10 tablets or less (After Intervention)	NR	765	1367 (68)	NR	NR	No
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site	Dispense quantity 10 tablets or less (After Intervention)	NR	464	410 (33.6)	NR	NR	No
Bachhuber, 2022[30]	Arm 1	Control	Dispense quantity 10 tablets or less	NR	1849	NR	NR	Ref	No
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site	Dispense quantity 10 tablets or less	NR	2775	NR	NR	Comparator: Arm 1 Difference in difference (percentage points): 38.7 (95% CI: 11.5 to 66), p = 0.003	No

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Outcome events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site	Dispense quantity 10 tablets or less	NR	1685	NR	NR	Comparator: Arm 1 Difference in difference (percentage points): 0.1 (95% CI: -5.8 to 6.1), p = 0.97	No

CI = confidence interval; N = sample size; NR = not reported

Evidence Table C-16. Pain intensity or distress outcome (continuous data) of included studies addressing effects of organizational leadership and policies within a healthcare facility or healthcare system

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	Sample Size (N)	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Ahmed, 2016[28]	Arm 1	Pre-protocol	Mean pre-treatment pain score	NR	Baseline: 50 Followup: 50	Mean: 8.4	NR	Comparator: Arm 2 and 3 Mean: p=0.04	No
Ahmed, 2016[28]	Arm 2	Post-protocol (cohort 1)	Mean pre-treatment pain score	NR	Baseline: 44 Followup: 44	Mean: 7.5	NR	Comparator: Arm 1 and 3 Mean: p=0.04	No
Ahmed, 2016[28]	Arm 3	Post-protocol (cohort 2)	Mean pre-treatment pain score	NR	Baseline: 50 Followup: 50	Mean: 8.6	NR	Comparator: Arm 1 and 2 Mean: p=0.63	No
Ahmed, 2016[28]	Arm 1	Pre-protocol	Mean post-treatment pain score	NR	Baseline: 50 Followup: 50	Mean: 3.9	NR	Comparator: Arm 2 and 3 Mean: p=0.24	No
Ahmed, 2016[28]	Arm 2	Post-protocol (cohort 1)	Mean post-treatment pain score	NR	Baseline: 44 Followup: 44	Mean: 3.2	NR	Comparator: Arm 1 and 3 Mean: p=0.24	No
Ahmed, 2016[28]	Arm 3	Post-protocol (cohort 2)	Mean post-treatment pain score	NR	Baseline: 50 Followup: 50	Mean: 3.7	NR	Comparator: Arm 1 and 2 Mean: p=0.69	NR

NR = not reported

Evidence Table C-17. Number of pills per prescription (continuous data) of primary studies addressing effects of organizational leadership and policies within a healthcare facility or healthcare system

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	Sample Size (N)	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Bachhuber, 2021[29]	Arm 1	Control	Average number of tablets prescribed (Pre-Intervention)	NR	Baseline: 3957 Followup: NR	Baseline: Mean 45.1 (SD 99.7) Followup: NR	NR	NR	NR
Bachhuber, 2021[29]	Arm 2	Intervention	Average number of tablets prescribed (Pre-Intervention)	NR	Baseline: 3560 Followup: NR	Baseline: Mean 32.2 (SD 68.7) Followup: NR	NR	NR	NR
Bachhuber, 2021[29]	Arm 1	Control	Average number of tablets prescribed (Post-Intervention)	NR	Baseline: 7651 Followup: NR	Baseline: Mean 34.7 (SD 79) Followup: NR	NR	NR	NR
Bachhuber, 2021[29]	Arm 2	Intervention	Average number of tablets prescribed (Post-Intervention)	NR	Baseline: 6163 Followup: NR	Baseline: Mean 25.3 (SD 56.9) Followup: NR	NR	NR	NR
Bachhuber, 2021[29]	Arm 1	Control	Median number of tablets prescribed (Pre-Intervention)	NR	Baseline: 3957 Followup: NR	Baseline: Median 15 (IQR 10 to 30) Followup: NR	NR	NR	NR
Bachhuber, 2021[29]	Arm 2	Intervention	Median number of tablets prescribed (Pre-Intervention)	NR	Baseline: 3560 Followup: NR	Baseline: Median 15 (IQR 10 to 20) Followup: NR	NR	NR	NR
Bachhuber, 2021[29]	Arm 1	Control	Median number of tablets prescribed (Post-Intervention)	NR	Baseline: 7651 Followup: NR	Baseline: Median 12 (IQR 10 to 20) Followup: NR	NR	NR	NR
Bachhuber, 2021[29]	Arm 2	Intervention	Median number of tablets prescribed (Post-Intervention)	NR	Baseline: 6163 Followup: NR	Baseline: Median 10 (IQR 10 to 20) Followup: NR	NR	NR	Site characteristics: Number of visits, number of new opioid analgesic

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	Sample Size (N)	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
									prescriptions, percentage of commercial insurance Provider characteristics: sex and years in practice Patient characteristics: age, sex, race/ethnicity, pain diagnosis category, mental health history, substance use disorder diagnosis
Bachhuber, 2021[29]	Arm 1	Control	Tablets prescribed	NR	Baseline: 11608 Followup: NR	NR	NR	Ref	Site characteristics: Number of visits, number of new opioid analgesic prescriptions, percentage of commercial insurance Provider characteristics: sex and years in practice Patient characteristics: age, sex, race/ethnicity, pain diagnosis category, mental health history,

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	Sample Size (N)	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
									substance use disorder diagnosis d
Bachhuber, 2021[29]	Arm 2	Intervention	Tablets prescribed	NR	Baseline: 9723 Followup: NR	NR	NR	Comparator: Arm 1 Difference in difference: -2.1 (95% CI: -3.3 to -0.9), p<0.001	NR
Bachhuber, 2021[29]	Arm 1	Control	Mean Total Tablets prescribed during the 30-day period after the index prescription (Pre-Intervention	NR	Baseline: 3957 Followup: NR	Baseline: Mean 52.1 (SD 115.1) Followup: NR	NR	NR	NR
Bachhuber, 2021[29]	Arm 2	Intervention	Mean Total Tablets prescribed during the 30-day period after the index prescription (Pre-Intervention	NR	Baseline: 3560 Followup: NR	Baseline: Mean 37.8 (SD 79.8) Followup: NR	NR	NR	NR
Bachhuber, 2021[29]	Arm 1	Control	Mean Total Tablets prescribed during the 30-day period after the index prescription (Post-Intervention)	NR	Baseline: 7651 Followup: NR	Baseline: Mean 40.9 (SD 92.4) Followup: NR	NR	NR	NR
Bachhuber, 2021[29]	Arm 2	Intervention	Mean Total Tablets prescribed during the 30-day period after the index prescription (Post-Intervention)	NR	Baseline: 6163 Followup: NR	Baseline: Mean 30.8 (SD 69.8) Followup: NR	NR	NR	NR

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	Sample Size (N)	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Bachhuber, 2021[29]	Arm 1	Control	Median Total Tablets prescribed during the 30-day period after the index prescription (Pre-Intervention)	NR	Baseline: 3957 Followup: NR	Baseline: Median 15 (IQR 12 to 40) Followup: NR	NR	NR	NR
Bachhuber, 2021[29]	Arm 2	Intervention	Median Total Tablets prescribed during the 30-day period after the index prescription (Pre-Intervention)	NR	Baseline: 3560 Followup: NR	Baseline: Median 15 (IQR 10 to 30) Followup: NR	NR	NR	NR
Bachhuber, 2021[29]	Arm 1	Control	Median Total Tablets prescribed during the 30-day period after the index prescription (Post-Intervention)	NR	Baseline: 7651 Followup: NR	Baseline: Median 15 (IQR 10 to 30) Followup: NR	NR	NR	NR
Bachhuber, 2021[29]	Arm 2	Intervention	Median Total Tablets prescribed during the 30-day period after the index prescription (Post-Intervention)	NR	Baseline: 6163 Followup: NR	Baseline: Median 12 (IQR 10 to 24) Followup: NR	NR	NR	Number of visits, number of new opioid analgesic prescriptions, percentage of commercial insurance, sex and years in practice, age, sex, race/ethnicity, pain diagnosis category, mental health history, substance use disorder diagnosis
Bachhuber, 2021[29]	Arm 1	Control	Total Tablets prescribed during	NR	Baseline: 11608	NR	NR	Ref	Number of visits, number of new

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	Sample Size (N)	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
			the 30-day period after the index prescription		Followup: NR				opioid analgesic prescriptions, percentage of commercial insurance, sex and years in practice, age, sex, race/ethnicity, pain diagnosis category, mental health history, substance use disorder diagnosis
Bachhuber, 2021[29]	Arm 2	Intervention	Total Tablets prescribed during the 30-day period after the index prescription	NR	Baseline: 9723 Followup: NR	NR	NR	Comparator: Arm 1 Difference in difference: -2.7 (95% CI: -4.8 to -0.6), p=0.01	NR
Bachhuber, 2022[30]	Arm 1	Control	Average Tablets Prescribed (Before Intervention)	NR	Baseline: 522 Followup: NR	Baseline: Mean 15.1 (SD 5.1) Followup: NR	NR	NR	NR
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site	Average Tablets Prescribed (Before Intervention)	NR	Baseline: 765 Followup: NR	Baseline: Mean 18.2 (SD 13.2) Followup: NR	NR	NR	NR
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site	Average Tablets Prescribed (Before Intervention)	NR	Baseline: 464 Followup: NR	Baseline: Mean 15.7 (SD 4.4) Followup: NR	NR	NR	NR
Bachhuber, 2022[30]	Arm 1	Control	Average Tablets Prescribed (After Intervention)	NR	Baseline: 522 Followup: NR	Baseline: Mean 12.8 (SD 5.8) Followup: NR	NR	NR	NR

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	Sample Size (N)	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site	Average Tablets Prescribed (After Intervention)	NR	Baseline: 765 Followup: NR	Baseline: Mean 11.9 (SD 4.2) Followup: NR	NR	NR	NR
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site	Average Tablets Prescribed (After Intervention)	NR	Baseline: 464 Followup: NR	Baseline: Mean 12.9 (SD 4.2) Followup: NR	NR	NR	NR
Bachhuber, 2022[30]	Arm 1	Control	Median Tablets Prescribed (Before Intervention)	NR	Baseline: 522 Followup: NR	Baseline: Median 15 (IQR 12 to 20) Followup: NR	NR	NR	NR
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site	Median Tablets Prescribed (Before Intervention)	NR	Baseline: 765 Followup: NR	Baseline: Median 20 (IQR 15 to 20) Followup: NR	NR	NR	NR
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site	Median Tablets Prescribed (Before Intervention)	NR	Baseline: 464 Followup: NR	Baseline: Median 15 (IQR 12 to 20) Followup: NR	NR	NR	NR
Bachhuber, 2022[30]	Arm 1	Control	Median Tablets Prescribed (After Intervention)	NR	Baseline: 522 Followup: NR	Baseline: Median 12 (IQR 10 to 15) Followup: NR	NR	NR	NR
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site	Median Tablets Prescribed (After Intervention)	NR	Baseline: 765 Followup: NR	Baseline: Median 10 (IQR 10 to 15) Followup: NR	NR	NR	NR
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site	Median Tablets Prescribed (After Intervention)	NR	Baseline: 464 Followup: NR	Baseline: Median 12 (IQR 10 to 15) Followup: NR	NR	NR	Provider characteristics (specialty, trainee status) and patient characteristics (age, sex, race/ethnicity)
Bachhuber, 2022[30]	Arm 1	Control	Tablets prescribed	NR	Baseline: 1849	NR	NR	Ref	Provider characteristics

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	Sample Size (N)	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
					Followup: NR				(specialty, trainee status) and patient characteristics (age, sex, race/ethnicity)
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site	Tablets prescribed	NR	Baseline: 2775 Followup: NR	NR	NR	Comparator: Arm 1 Difference in difference: -3.3 (95% CI: -5.9 to -0.7), p=0.01	Provider characteristics (specialty, trainee status) and patient characteristics (age, sex, race/ethnicity)
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site	Tablets prescribed	NR	Baseline: 1685 Followup: NR	NR	NR	Comparator: Arm 1 Difference in difference: -0.2 (95% CI: -0.7 to 0.2), p=0.26	NR
Bachhuber, 2022[30]	Arm 1	Control	Mean Total Tablets prescribed during the 30-day period after the index prescription (Before Intervention)	NR	Baseline: 522 Followup: NR	Baseline: Mean 16.8 (SD 8.2) Followup: NR	NR	NR	NR
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site	Mean Total Tablets prescribed during the 30-day period after the index prescription (Before Intervention)	NR	Baseline: 765 Followup: NR	Baseline: Mean 19.6 (SD 15.1) Followup: NR	NR	NR	NR

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	Sample Size (N)	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site	Mean Total Tablets prescribed during the 30-day period after the index prescription (Before Intervention)	NR	Baseline: 464 Followup: NR	Baseline: Mean 17.2 (SD 7.4) Followup: NR	NR	NR	NR
Bachhuber, 2022[30]	Arm 1	Control	Mean Total Tablets prescribed during the 30-day period after the index prescription (After Intervention)	NR	Baseline: 522 Followup: NR	Baseline: Mean 13.9 (SD 7.7) Followup: NR	NR	NR	NR
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site	Mean Total Tablets prescribed during the 30-day period after the index prescription (After Intervention)	NR	Baseline: 765 Followup: NR	Baseline: Mean 12.8 (SD 6) Followup: NR	NR	NR	NR
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site	Mean Total Tablets prescribed during the 30-day period after the index prescription (After Intervention)	NR	Baseline: 464 Followup: NR	Baseline: Mean 14.2 (SD 6.9) Followup: NR	NR	NR	NR
Bachhuber, 2022[30]	Arm 1	Control	Median Total Tablets prescribed during the 30-day period after the index prescription (Before Intervention)	NR	Baseline: 522 Followup: NR	Baseline: Median 15 (IQR 12 to 20) Followup: NR	NR	NR	NR

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	Sample Size (N)	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site	Median Total Tablets prescribed during the 30-day period after the index prescription (Before Intervention)	NR	Baseline: 765 Followup: NR	Baseline: Median 20 (IQR 15 to 20) Followup: NR	NR	NR	NR
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site	Median Total Tablets prescribed during the 30-day period after the index prescription (Before Intervention)	NR	Baseline: 464 Followup: NR	Baseline: Median 15 (IQR 15 to 20) Followup: NR	NR	NR	NR
Bachhuber, 2022[30]	Arm 1	Control	Median Total Tablets prescribed during the 30-day period after the index prescription (After Intervention)	NR	Baseline: 522 Followup: NR	Baseline: Median 12 (IQR 10 to 15) Followup: NR	NR	NR	NR
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site	Median Total Tablets prescribed during the 30-day period after the index prescription (After Intervention)	NR	Baseline: 765 Followup: NR	Baseline: Median 10 (IQR 10 to 15) Followup: NR	NR	NR	NR
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site	Median Total Tablets prescribed during the 30-day period after the index prescription (After Intervention)	NR	Baseline: 464 Followup: NR	Baseline: Median 15 (IQR 10 to 15) Followup: NR	NR	NR	Provider characteristics (specialty, trainee status) and patient characteristics (age, sex, race/ethnicity)

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	Sample Size (N)	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Bachhuber, 2022[30]	Arm 1	Control	Total Tablets prescribed during the 30-day period after the index prescription	NR	Baseline: 1849 Followup: NR	NR	NR	Ref	Provider characteristics (specialty, trainee status) and patient characteristics (age, sex, race/ethnicity)
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site	Total Tablets prescribed during the 30-day period after the index prescription	NR	Baseline: 2775 Followup: NR	NR	NR	Comparator: Arm 1 Difference in difference: -3.3 (95% CI: -5.6 to -1), p=0.002	Provider characteristics (specialty, trainee status) and patient characteristics (age, sex, race/ethnicity)
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site	Total Tablets prescribed during the 30-day period after the index prescription	NR	Baseline: 1685 Followup: NR	NR	NR	Comparator: Arm 1 Difference in difference: 0.1 (95% CI: -0.7 to 0.9), p=0.85	NR
Bachhuber, 2022[30]	Arm 1	Control	Average Total MME prescribed during the 30-day period after the index prescription (Before Intervention)	NR	Baseline: 522 Followup: NR	Baseline: Mean 98.4 (SD 69.7) Followup: NR	NR	NR	NR
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site	Average Total MME prescribed during the 30-day period after the index prescription (Before Intervention)	NR	Baseline: 765 Followup: NR	Baseline: Mean 95.4 (SD 79.5) Followup: NR	NR	NR	NR

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	Sample Size (N)	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site	Average Total MME prescribed during the 30-day period after the index prescription (Before Intervention)	NR	Baseline: 464 Followup: NR	Baseline: Mean 103.4 (SD 68.1) Followup: NR	NR	NR	NR
Bachhuber, 2022[30]	Arm 1	Control	Average Total MME prescribed during the 30-day period after the index prescription (After Intervention)	NR	Baseline: 522 Followup: NR	Baseline: Mean 78.8 (SD 80.4) Followup: NR	NR	NR	NR
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site	Average Total MME prescribed during the 30-day period after the index prescription (After Intervention)	NR	Baseline: 765 Followup: NR	Baseline: Mean 62 (SD 34.4) Followup: NR	NR	NR	NR
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site	Average Total MME prescribed during the 30-day period after the index prescription (After Intervention)	NR	Baseline: 464 Followup: NR	Baseline: Mean 84.7 (SD 59.5) Followup: NR	NR	NR	NR
Bachhuber, 2022[30]	Arm 1	Control	Median Total MME prescribed during the 30-day period after the index prescription (Before Intervention)	NR	Baseline: 522 Followup: NR	Baseline: Median 90 (IQR 67.5 to 112.5) Followup: NR	NR	NR	NR
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site	Median Total MME prescribed during the 30-day	NR	Baseline: 765	Baseline: Median 90 (IQR 67.5 to	NR	NR	NR

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	Sample Size (N)	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
			period after the index prescription (Before Intervention)		Followup: NR	90) Followup: NR			
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site	Median Total MME prescribed during the 30-day period after the index prescription (Before Intervention)	NR	Baseline: 464 Followup: NR	Baseline: Median 90 (IQR 67.5 to 112.5) Followup: NR	NR	NR	NR
Bachhuber, 2022[30]	Arm 1	Control	Median Total MME prescribed during the 30-day period after the index prescription (After Intervention)	NR	Baseline: 522 Followup: NR	Baseline: Median 67.5 (IQR 45 to 90) Followup: NR	NR	NR	NR
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site	Median Total MME prescribed during the 30-day period after the index prescription (After Intervention)	NR	Baseline: 765 Followup: NR	Baseline: Median 45 (IQR 45 to 75) Followup: NR	NR	NR	NR
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site	Median Total MME prescribed during the 30-day period after the index prescription (After Intervention)	NR	Baseline: 464 Followup: NR	Baseline: Median 67.5 (IQR 54 to 112.5) Followup: NR	NR	NR	Provider characteristics (specialty, trainee status) and patient characteristics (age, sex, race/ethnicity)
Bachhuber, 2022[30]	Arm 1	Control	Total MME prescribed during the 30-day period after the index prescription	NR	Baseline: 1849 Followup: NR	NR	NR	Ref	Provider characteristics (specialty, trainee status) and patient characteristics

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	Sample Size (N)	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
									(age, sex, race/ethnicity)
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site	Total MME prescribed during the 30-day period after the index prescription	NR	Baseline: 2775 Followup: NR	NR	NR	Comparator: Arm 1 Difference in difference: -15.7 (95% CI: -28.1 to -3.3), p=0.008	Provider characteristics (specialty, trainee status) and patient characteristics (age, sex, race/ethnicity)
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site	Total MME prescribed during the 30-day period after the index prescription	NR	Baseline: 1685 Followup: NR	NR	NR	Comparator: Arm 1 Difference in difference: 3.1 (95% CI: -5.1 to 11.2), p=0.46	NR

CI = confidence interval; IQR = interquartile range; MME = morphine milligram equivalent; NR = not reported; Ref = reference; SD = standard deviation

Evidence Table C-18. Total morphine milligram equivalents per prescription (continuous data) of primary studies addressing effects of organizational leadership and policies within a healthcare facility or healthcare system

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	Samples Size (N)	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Bachhuber, 2021[29]	Arm 1	Control	Average MME prescribed (Pre-Intervention	NR	Baseline: 3957 Followup: NR	Baseline: Mean 253.8 (SD 511.2) Followup: NR	NR	NR	NR
Bachhuber, 2021[29]	Arm 2	Intervention	Average MME prescribed (Pre-Intervention)	NR	Baseline: 3560 Followup: NR	Baseline: Mean 184.9 (SD 365.5) Followup: NR	NR	NR	NR

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	Samples Size (N)	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Bachhuber, 2021[29]	Arm 1	Control	Average MME prescribed (Post-Intervention)	NR	Baseline: 7651 Followup: NR	Baseline: Mean 197.8 (SD 406.8) Followup: NR	NR	NR	NR
Bachhuber, 2021[29]	Arm 2	Intervention	Average MME prescribed (Post-Intervention)	NR	Baseline: 6163 Followup: NR	Baseline: Mean 144.9 (SD 298.2) Followup: NR	NR	NR	NR
Bachhuber, 2021[29]	Arm 1	Control	Median MME prescribed (Pre-Intervention)	NR	Baseline: 3957 Followup: NR	Baseline: Median 90 (IQR 75 to 150) Followup: NR	NR	NR	NR
Bachhuber, 2021[29]	Arm 2	Intervention	Median MME prescribed (Pre-Intervention)	NR	Baseline: 3560 Followup: NR	Baseline: Median 90 (IQR 67.5 to 150) Followup: NR	NR	NR	NR
Bachhuber, 2021[29]	Arm 1	Control	Median MME prescribed (Post-Intervention)	NR	Baseline: 7651 Followup: NR	Baseline: Median 90 (IQR 60 to 150) Followup: NR	NR	NR	NR

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	Samples Size (N)	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Bachhuber, 2021[29]	Arm 2	Intervention	Median MME prescribed (Post-Intervention)	NR	Baseline: 6163 Followup: NR	Baseline: Median 75 (IQR 50 to 112.5) Followup: NR	NR	NR	Number of visits, number of new opioid analgesic prescriptions, percentage of commercial insurance, sex and years in practice, age, sex, race/ethnicity, pain diagnosis category, mental health history, substance use disorder diagnosis

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	Samples Size (N)	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Bachhuber, 2021[29]	Arm 1	Control	MME Prescribed	NR	Baseline: 11608 Followup: NR	NR	NR	Ref	Number of visits, number of new opioid analgesic prescriptions, percentage of commercial insurance, sex and years in practice, age, sex, race/ethnicity, pain diagnosis category, mental health history, substance use disorder diagnosis
Bachhuber, 2021[29]	Arm 2	Intervention	MME Prescribed	NR	Baseline: 9723 Followup: NR	NR	NR	Comparator: Arm 1 Difference in difference: -14.6 (95% CI: -22.6 to -6.6), p<0.001	NR
Bachhuber, 2021[29]	Arm 1	Control	Mean Total MME prescribed during the 30-day period after the index prescription (Pre-Intervention)	NR	Baseline: 3957 Followup: NR	Baseline: Mean 304.9 (SD 650.8) Followup: NR	NR	NR	NR

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	Samples Size (N)	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Bachhuber, 2021[29]	Arm 2	Intervention	Mean Total MME prescribed during the 30-day period after the index prescription (Pre-Intervention)	NR	Baseline: 3560 Followup: NR	Baseline: Mean 229.6 (SD 494.5) Followup: NR	NR	NR	NR
Bachhuber, 2021[29]	Arm 1	Control	Mean Total MME prescribed during the 30-day period after the index prescription (Post-Intervention)	NR	Baseline: 7651 Followup: NR	Baseline: Mean 244.7 (SD 564.6) Followup: NR	NR	NR	NR
Bachhuber, 2021[29]	Arm 2	Intervention	Mean Total MME prescribed during the 30-day period after the index prescription (Post-Intervention)	NR	Baseline: 6163 Followup: NR	Baseline: Mean 186.4 (SD 501.6) Followup: NR	NR	NR	NR
Bachhuber, 2021[29]	Arm 1	Control	Median Total MME prescribed during the 30-day period after the index prescription (Pre-Intervention)	NR	Baseline: 3957 Followup: NR	Baseline: Median 100 (IQR 75 to 225) Followup: NR	NR	NR	NR
Bachhuber, 2021[29]	Arm 2	Intervention	Median Total MME prescribed during the 30-day period after the index prescription (Pre-Intervention)	NR	Baseline: 3560 Followup: NR	Baseline: Median 90 (IQR 75 to 180) Followup: NR	NR	NR	NR

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	Samples Size (N)	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Bachhuber, 2021[29]	Arm 1	Control	Median Total MME prescribed during the 30-day period after the index prescription (Post-Intervention)	NR	Baseline: 7651 Followup: NR	Baseline: Median 90 (IQR 67.5 to 172.5) Followup: NR	NR	NR	NR
Bachhuber, 2021[29]	Arm 2	Intervention	Median Total MME prescribed during the 30-day period after the index prescription (Post-Intervention)	NR	Baseline: 6163 Followup: NR	Baseline: Median 75 (IQR 52.5 to 150) Followup: NR	NR	NR	Number of visits, number of new opioid analgesic prescriptions, percentage of commercial insurance, sex and years in practice, age, sex, race/ethnicity, pain diagnosis category, mental health history, substance use disorder diagnosis

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	Samples Size (N)	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Bachhuber, 2021[29]	Arm 1	Control	Total MME prescribed during the 30-day period after the index prescription	NR	Baseline: 11608 Followup: NR	NR	NR	Ref	Number of visits, number of new opioid analgesic prescriptions, percentage of commercial insurance, sex and years in practice, age, sex, race/ethnicity, pain diagnosis category, mental health history, substance use disorder diagnosis
Bachhuber, 2021[29]	Arm 2	Intervention	Total MME prescribed during the 30-day period after the index prescription	NR	Baseline: 9723 Followup: NR	NR	NR	Comparator: Arm 1 Difference in difference: -15.8 (95% CI: -33.8 to 2.2), p=0.09	NR
Bachhuber, 2022[30]	Arm 1	Control	Average MME Prescribed (Pre-Intervention)	NR	Baseline: 522 Followup: NR	Baseline: Mean 86.8 (SD 40.9) Followup: NR	NR	NR	NR
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site	Average MME Prescribed (Pre-Intervention)	NR	Baseline: 765 Followup: NR	Baseline: Mean 87.2 (SD 61.6) Followup: NR	NR	NR	NR

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	Samples Size (N)	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site	Average MME Prescribed (Pre-Intervention)	NR	Baseline: 464 Followup: NR	Baseline: Mean 93.5 (SD 47) Followup: NR	NR	NR	NR
Bachhuber, 2022[30]	Arm 1 - Usual Care	Control	Average MME Prescribed (Post-Intervention)	NR	Baseline: 522 Followup: NR	Baseline: Mean 69.8 (SD 41.7) Followup: NR	NR	NR	NR
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site	Average MME Prescribed (Post-Intervention)	NR	Baseline: 765 Followup: NR	Baseline: Mean 57.1 (SD 24.1) Followup: NR	NR	NR	NR
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site	Average MME Prescribed (Post-Intervention)	NR	Baseline: 464 Followup: NR	Baseline: Mean 76.7 (SD 44.1) Followup: NR	NR	NR	NR
Bachhuber, 2022[30]	Arm 1	Control	Median MME Prescribed (Pre-Intervention)	NR	Baseline: 522 Followup: NR	Baseline: Median 75 (IQR 67.5 to 112.5) Followup: NR	NR	NR	NR
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site	Median MME Prescribed (Pre-Intervention)	NR	Baseline: 765 Followup: NR	Baseline: Median 90 (IQR 67.5 to 90) Followup: NR	NR	NR	NR
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site		NR	Baseline: 464 Followup: NR	Baseline: Median 90 (IQR 67.5 to 112.5) Followup: NR	NR	NR	NR
Bachhuber, 2022[30]	Arm 1	Control	Median MME Prescribed (Post-Intervention)	NR	Baseline: 522 Followup: NR	Baseline: Median 67.5 (IQR 45 to 90) Followup: NR	NR	NR	NR

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	Samples Size (N)	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site	Median MME Prescribed (Post-Intervention)	NR	Baseline: 765 Followup: NR	Baseline: Median 45 (IQR 45 to 67.5) Followup: NR	NR	NR	NR
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site	Median MME Prescribed (Median MME Prescribed (Post-Intervention) Intervention)	NR	Baseline: 464 Followup: NR	Baseline: Median 67.5 (IQR 50 to 90) Followup: NR	NR	NR	Provider characteristics (specialty, trainee status) and patient characteristics (age, sex, race/ethnicity)
Bachhuber, 2022[30]	Arm 1	Control	MME Prescribed	NR	Baseline: 1849 Followup: NR	NR	NR	Ref	Provider characteristics (specialty, trainee status) and patient characteristics (age, sex, race/ethnicity)
Bachhuber, 2022[30]	Arm 2	10-Tablet Default Site	MME Prescribed	NR	Baseline: 2775 Followup: NR	NR	NR	Comparator: Arm 1 Difference in difference: -14.1 (95% CI: -27.8 to -0.4), p=0.04	Provider characteristics (specialty, trainee status) and patient characteristics (age, sex, race/ethnicity)
Bachhuber, 2022[30]	Arm 3	5-Tablet Default Site	MME Prescribed	NR	Baseline: 1685 Followup: NR	NR	NR	Comparator: Arm 1 Difference in difference: 2.4 (95% CI: -1.4 to 6.2), p=0.22	NR

CI = confidence interval; IQR = interquartile range; MME = morphine milligram equivalent; N = sample size; NR = not reported; Ref = reference; SD = standard deviation

Evidence Table C-19. Opioid refill request (categorical data) of primary studies addressing effects of clinical knowledge, expertise, and behavior interventions related to prescribed or ordered opioids

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Outcome Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Sada, 2019[31]	Arm 1	Phase 1	No. of patient requiring refills	NR	16	2 (NR)	NR	NR	No
Sada, 2019[31]	Arm 2	Phase 2	No. of patient requiring refills	NR	23	1 (NR)	NR	NR	No
Sada, 2019[31]	Arm 3	Phase 3	No. of patient requiring refills	NR	22	5 (NR)	NR	NR	No
Sada, 2019[31]	Arm 4	Phase 4	No. of patient requiring refills	NR	27	2 (NR)	NR	NR	No

N = sample size; NR = not reported

Evidence Table C-20. Patient satisfaction (categorical data) of primary studies addressing effects of clinical knowledge, expertise, and behavior interventions related to prescribed or ordered opioids

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Outcome Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Sada, 2019[31]	Arm 1	Phase 1	Satisfaction	NR	16	NR (93)	NR	NR	No
Sada, 2019[31]	Arm 2	Phase 2	Satisfaction	NR	23	NR (83)	NR	NR	No
Sada, 2019[31]	Arm 3	Phase 3	Satisfaction	NR	22	NR (73)	NR	NR	No
Sada, 2019[31]	Arm 4	Phase 4	Satisfaction	NR	27	NR (93)	NR	NR	No

N = sample size; NR = not reported

Evidence Table C-21. Number of pills per prescription (continuous data) of primary studies addressing effects of clinical knowledge, expertise, and behavior interventions related to prescribed or ordered opioids

Author, Year	Arm	Arm Name	Outcome Definition*	Time Point at Analysis	N	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Sada, 2019[31]	Arm 1	Phase 1	Average Prescribed No. of Tablets - High Risk patients (5-mg oxycodone or 50-mg tramadol)	NR	Baseline: NR Followup: NR	Oxycodone: 42 Tramadol: 12	NR	NR	No
Sada, 2019[31]	Arm 2	Phase 2	Average Prescribed No. of Tablets - High Risk patients (5-mg oxycodone or 50-mg tramadol)	NR	Baseline: NR Followup: NR	Oxycodone: 40 Tramadol: 60	NR	NR	No
Sada, 2019[31]	Arm 3	Phase 3	Average Prescribed No. of Tablets - High Risk patients (5-mg oxycodone or 50-mg tramadol)	NR	Baseline: NR Followup: NR	Oxycodone: 20 Tramadol: 30	NR	NR	No
Sada, 2019[31]	Arm 4	Phase 4	Average Prescribed No. of Tablets - High Risk patients (5-mg oxycodone or 50-mg tramadol)	NR	Baseline: NR Followup: NR	Oxycodone: 23 Tramadol: 34	NR	NR	No
Sada, 2019[31]	Arm 1	Phase 1	Average Prescribed No. of Tablets - Low Risk patients (5-mg oxycodone or 50-mg tramadol)	NR	Baseline: NR Followup: NR	Oxycodone: 42 Tramadol 12	NR	NR	No
Sada, 2019[31]	Arm 2	Phase 2	Average Prescribed No. of Tablets - Low Risk patients (5-mg oxycodone or 50-mg tramadol)	NR	Baseline: NR Followup: NR	Oxycodone 20 Tramadol 40	NR	NR	No
Sada, 2019[31]	Arm 3	Phase 3	Average Prescribed No. of Tablets - Low Risk patients (5-mg oxycodone or 50-mg tramadol)	NR	Baseline: NR Followup: NR	Oxycodone: 12 Tramadol: 20	NR	NR	No
Sada, 2019[31]	Arm 4	Phase 4	Average Prescribed No. of Tablets - Low Risk patients (5-mg oxycodone or 50-mg tramadol)	NR	Baseline: NR Followup: NR	Oxycodone: 18 Tramadol: 32	NR	NR	No

mg = milligram; N = sample size; NR = not reported

* Patients were considered high risk for postmastectomy pain if they were 65 years of age or less, hospitalization opioid consumption was greater than 6, 5-mg oxycodone pills, and if their pain scores were frequently >7. Criteria for patients considered low risk was not specified.

Evidence Table C-22. Total morphine milligram equivalents per prescription (continuous data) of primary studies addressing effects of clinical knowledge, expertise, and behavior interventions related to prescribed or ordered opioids

Author, Year	Arm	Arm Name	Outcome Definition*	Time Point at Analysis	N	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Sada, 2019[31]	Arm 1	Phase 1	Median MME Prescribed per patient (average risk & high risk)	NR	Baseline: 16 Followup: NR	Average risk: 450 MME High risk: not available	NR	NR	No
Sada, 2019[31]	Arm 2	Phase 2	Median MME Prescribed (average risk & high risk)	NR	Baseline: 23 Followup: NR	Average risk: 550 MME High risk: 900	NR	NR	No
Sada, 2019[31]	Arm 3	Phase 3	Median MME Prescribed (average risk & high risk)	NR	Baseline: 22 Followup: NR	Average risk: 290 MME High risk: 450 MME	NR	NR	No
Sada, 2019[31]	Arm 4	Phase 4	Median MME Prescribed (average risk & high risk)	NR	Baseline: 27 Followup: NR	Average risk: 263 MME High risk: 425 MME	NR	NR	No

MME = morphine milligram equivalent; N = sample size; NR = not reported

*Not specified by study authors on whether dose per day or total per prescription

Evidence Table C-23. Healthcare utilization outcome (categorical data) of primary studies addressing effects of patient and family education or engagement related to use of prescribed or ordered opioids

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Delara, 2022[36]	Arm 1	Standard	Unexpected visits to the emergency department due to uncontrolled pain	NR	32	0 (0)	NR	Ref	No
Delara, 2022[36]	Arm 2	Patient-directed	Unexpected visits to the emergency department due to uncontrolled pain	NR	33	2 (6.1)	NR	Comparator: Arm 1 p-value only: p = 0.49	No
Delara, 2022[36]	Arm 1	Standard	Unexpected visits to the office due to uncontrolled pain	NR	32	1 (3.1)	NR	Ref	No
Delara, 2022[36]	Arm 2	Patient-directed	Unexpected visits to the office due to uncontrolled pain	NR	33	1 (3)	NR	Comparator: Arm 1 p-value only: p = >0.99	No
Voelpel-Lewis, 2021[34]	Arm 1	Control	Serious adverse events (those that led to a call or unplanned return visit to the clinic or hospital setting)	NR	292	10 (3.4)	NR	Ref	No
Voelpel-Lewis, 2021[34]	Arm 2	STOMP	Serious adverse events (those that led to a call or unplanned return visit to the clinic or hospital setting)	NR	271	9 (3.3)	NR	Comparator: Arm 1 Odds ratio: 0.93 (95% CI: 0.37 to 2.33), p = NR	No

CI = confidence interval; N = sample size; NR = not reported; Ref = reference; STOMP = Scenario-Tailored Opioid Messaging Program

Evidence Table C-24. Opioid refill request (categorical data) of primary studies addressing effects of patient and family education or engagement related to use of prescribed or ordered opioids

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Outcome Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Delara, 2022[36]	Arm 1	Standard	Number of patients prescribed additional oxycodone after preoperative visit	NR	32	0 (0)	NR	Ref	No
Delara, 2022[36]	Arm 2	Patient-directed	Number of patients prescribed additional oxycodone after preoperative visit	NR	33	5 (15.2)	NR	Comparator: Arm 1 p-value only: p = 0.05	No
Egan, 2020[33]	Arm 1	Control	Required a prescription refill	NR	46	10 (22)	NR	Ref	No
Egan, 2020[33]	Arm 2	Intervention	Required a prescription refill	NR	39	6 (15)	NR	Comparator: Arm 1 p-value only: p = 0.3	No
Stepan, 2021[35]	Arm 1	Control	Refilled prescription	15 days	98	9 (10.5)	NR	Ref	No
Stepan, 2021[35]	Arm 2	Education	Refilled prescription	15 days	93	2 (2.6)	NR	Comparator: Arm 1 p-value only: p = 0.046	No

N = sample size; NR = not reported; Ref = reference

Evidence Table C-25. Opioid refill request (continuous data) of primary studies addressing effects of patient and family education or engagement related to use of prescribed or ordered opioids

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Delara, 2022[36]	Arm 1	Standard	Number of additional oxycodone tablets prescribed after preoperative visit	After pre-operative visit	Baseline: 32 Followup: 32	Baseline: NR Followup: Median 0 (IQR NR)	NR	NR	NR
Delara, 2022[36]	Arm 2	Patient-directed	Number of additional oxycodone tablets prescribed after preoperative visit	After pre-operative visit	Baseline: 33 Followup: 33	Baseline: NR Followup: Median 10 (IQR 10,15)	NR	NR	NR
Egan, 2020[33]	Arm 1	Control	Total opioid tablets prescribed with refills	NR	Baseline: 50 Followup: 46	Baseline: NR Followup: Mean 46.6 (SD 21.8)	NR	Ref	NR
Egan, 2020[33]	Arm 2	Intervention	Total opioid tablets prescribed with refills	NR	Baseline: 50 Followup: 39 bs	Baseline: NR Followup: Mean 39.2 (SD 11.9)	NR	Comparator: Arm 1 p-value only: p=0.04	NR
Long, 2022[37]	Arm 1	Standard	Opioid refills	NR	Baseline: 40 Followup: 40	Baseline: NR Followup: Count 1 (NR)	NR	NR	NR
Long, 2022[37]	Arm 2	Restricted	Opioid refills	NR	Baseline: 42 Followup: 42	Baseline: NR Followup: Count 1 (NR)	NR	NR	NR

IQR = interquartile range; N = sample size; NR = not reported; Ref = reference; SD = standard deviation

Evidence Table C-26. Patient satisfaction (categorical data) of primary studies addressing effects of patient and family education or engagement related to use of prescribed or ordered opioids

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Outcome Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Delara, 2022[36]	Arm 1	Standard	Satisfied	NR	32	27 (87.1)	NR	Ref	No
Delara, 2022[36]	Arm 2	Patient-directed	Satisfied	NR	33	29 (90.6)	NR	Comparator: Arm 1 p-value only: p = 0.66	No
Stepan, 2021[35]	Arm 1	Control	Dissatisfied	15 days	98	7 (8.2)	NR	Ref	No
Stepan, 2021[35]	Arm 2	Education	Dissatisfied	15 days	93	1 (1.3)	NR	Comparator: Arm 1 p-value only: p = 0.03	No
Stepan, 2021[35]	Arm 1	Control	Satisfied	15 days	98	78 (91.8)	NR	Ref	No
Stepan, 2021[35]	Arm 2	Education	Satisfied	15 days	93	73 (94.8)	NR	Comparator: Arm 1 p-value only: p = 0.03	No
Stepan, 2021[35]	Arm 1	Control	Neutral	15 days	98	0 (0)	NR	Ref	No
Stepan, 2021[35]	Arm 2	Education	Neutral	15 days	93	3 (3.9)	NR	Comparator: Arm 1 p-value only: p = 0.03	No

N = sample size; NR = not reported; Ref = reference

Evidence Table C-27. Patient satisfaction (continuous data) of primary studies addressing effects of patient and family education or engagement related to use of prescribed or ordered opioids

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Long, 2022[37]	Arm 1	Standard	Mean pain control satisfaction score	NR	Baseline: 40 Followup: 40	Baseline: NR Followup: Mean 4.1 (SD 0.8)	NR	Ref	NR
Long, 2022[37]	Arm 2	Restricted	Mean pain control satisfaction score	NR	Baseline: 42 Followup: 42	Baseline: NR Followup: Mean 4 (SD 0.9)	NR	Comparator: Arm 1 p-value only: p=0.3	NR

N = sample size; NR = not reported; Ref = reference; SD = standard deviation

Evidence Table C-28. Rates of opioid prescribing (categorical data) of studies addressing effects of patient and family education or engagement related to use of prescribed or ordered opioids

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Outcome Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Long, 2022[37]	Arm 1	Standard	Patients who filled an opioid prescription	NR	40	23 (57.5)	NR	Ref	No
Long, 2022[37]	Arm 2	Restricted	ents who filled an opioid prescription	NR	42	8 (19)	NR	Comparator: Arm 1 p-value only: $p < 0.001$	No

N = sample size; NR = not reported; Ref = reference

Evidence Table C-29. Rates of opioid prescribing (continuous data) of primary studies addressing effects of patient and family education or engagement related to use of prescribed or ordered opioids

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Egan, 2020[33]	Arm 1	Control	Postoperative opioid "prescription number"	NR	Baseline: 50 Followup: 46	Baseline: NR Followup: Mean 36.8 (SD 6.7)	NR	Ref	NR
Egan, 2020[33]	Arm 2	Intervention	Postoperative opioid "prescription number"	NR	Baseline: 50 Followup: 39	Baseline: NR Followup: Mean 35.3 (SD 5.5)	NR	Comparator: Arm 1 p-value only: p=0.2	NR
Voelpel-Lewis, 2021[34]	Arm 1	Control	Opioid doses dispensed	NR	Baseline: 308 Followup: 292	Baseline: NR Followup: Mean 21.5 (SD 13.76)	NR	Ref	NR
Voelpel-Lewis, 2021[34]	Arm 2	STOMP	Opioid doses dispensed	NR	Baseline: 296 Followup: 271	Baseline: NR Followup: Mean 22 (SD 16.48)	NR	Comparator: Arm 1 Mean difference: 0.5 (95% CI: -1.95 to 2.96), p=NR	NR

CI = confidence interval; N = sample size; NR = not reported; Ref = reference; SD = standard deviation; STOMP = Scenario-Tailored Opioid Messaging Program

Evidence Table C-30. Pain intensity or distress outcome (continuous data) of primary studies addressing effects of patient and family education or engagement related to use of prescribed or ordered opioids

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Egan, 2020[33]	Arm 1	Control	Acceptable postoperative pain level	13 days	Baseline: 50 Followup: 46	Baseline: NR Followup: Mean 3 (SD 1.6)	NR	Ref	NR
Egan, 2020[33]	Arm 2	Intervention	Acceptable postoperative pain level	13 days	Baseline: 50 Followup: 39	Baseline: NR Followup: Mean 3.1 (SD 1.4)	NR	Comparator: Arm 1 p-value only: p=0.7	NR
Egan, 2020[33]	Arm 1	Control	Average postoperative pain score	13 days	Baseline: 50 Followup: 46	Baseline: NR Followup: Mean 3.6 (SD 1.6)	NR	Ref	NR
Egan, 2020[33]	Arm 2	Intervention	Average postoperative pain score	13 days	Baseline: 50 Followup: 39	Baseline: NR Followup: Mean 3 (SD 1.8)	NR	Comparator: Arm 1 p-value only: p=0.06	NR
Long, 2022[37]	Arm 1	Standard	Mean pain scores [days 1 - 7]	Days 1 - 7	Baseline: 40 Followup: 40	Baseline: NR Followup Mean Day 0: 4.11 Day 1: 3.7 Day 2: 2.97 Day 3: 2.45 Day 4: 1.97 Day 5: 1.36 Day 6: 1.60 Day 7: 1.06	NR	Ref	NR

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Long, 2022[37]	Arm 2	Restricted	Mean pain scores [days 1 - 7]	Days 1 - 7	Baseline: 42 Followup: 42	Baseline: NR Followup Mean: Day 0: 4.37 Day 1: 3.93 Day 2: 2.98 Day 3: 2.45 Day 4: 1.81 Day 5: 1.82 Day 6: 1.39 Day 7: 1.48	NR	Comparator: Arm 1 p-value only: p=0.60; 0.64; 0.98; 1;0.75;0.36;0.67;0.40	NR
Stepan, 2021[35]	Arm 1	Control	Average pain at week 1	1 week	Baseline: 98 Followup: 98	Baseline: NR Followup: Median 3.6 (Range 0-9.1)	NR	Ref	NR
Stepan, 2021[35]	Arm 2	Education	Average pain at weak 1	1 week	Baseline: 93 Followup: 93	Baseline: NR Followup: Median 3.3 (Range 0-9.3)	NR	Comparator: Arm 1 p-value only: p=0.27	NR
Syed, 2018[32]	Arm 1	Control	VAS pain score at 2 weeks	2 weeks	Baseline: 66 Followup: NR	Baseline: NR Followup: Mean 4.4 (SD 2.5)	NR	Ref	NR
Syed, 2018[32]	Arm 2	Study	VAS pain score at 2 weeks	2 weeks	Baseline: 68 Followup: NR	Baseline: NR Followup: Mean 3.3 (SD 2.2)	NR	Comparator: Arm 1 p-value only: p=0.008	NR
Syed, 2018[32]	Arm 1	Control	VAS pain score at 6 weeks	6 weeks	Baseline: 66 Followup: NR	Baseline: NR Followup: Mean 3.7 (SD 2.4)	NR	Ref	NR
Syed, 2018[32]	Arm 2	Study	VAS pain score at 6 weeks	6 weeks	Baseline: 68 Followup: NR	Baseline: NR Followup: Mean 2.4 (SD 2)	NR	Comparator: Arm 1 p-value only: p=0.001	NR
Syed, 2018[32]	Arm 1	Control	VAS pain score at 3 months	3 months	Baseline: 66 Followup: NR	Baseline: NR Followup: Mean 2.2 (SD 2.2)	NR	Ref	NR

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Syed, 2018[32]	Arm 2	Study	VAS pain score at 3 months	3 months	Baseline: 68 Followup: NR	Baseline: NR Followup: Mean 2.2 (SD 2.4)	NR	Comparator: Arm 1 p-value only: p=0.2	NR
Voelpel-Lewis, 2021[34]	Arm 1	Control	Child self-reported pain scores [Days 1-3; 4-7; 8-14]	Days 1 - 3; 4 - 7; 8 - 14	Baseline: 308 Followup: 292	Baseline: NR Followup: Mean 4.9; 3.8; 3.2 (SD 2;1.8;1.9)	NR	Ref	NR
Voelpel-Lewis, 2021[34]	Arm 2	STOMP	Child self-reported pain scores [Days 1-3; 4-7; 8-14]	Days 1 - 3; 4 - 7; 8 - 15	Baseline: 296 Followup: 271	Baseline: NR Followup: Mean 4.9; 4;3.5 (SD 2;2.1;2.3)	NR	Comparator: Arm 1 Mean difference: 1.1;0.16;0.30 (95% CI: -0.36 to 0.33; -0.23 to 0.54; -0.23 ro 0.83), p=NR	NR
Voelpel-Lewis, 2021[34]	Arm 1	Control	Parent-reported pain interference score day 14	Day 14	Baseline: 308 Followup: 292	Baseline: NR Followup: Mean 8.06 (SD 8.06)	NR	Ref	NR
Voelpel-Lewis, 2021[34]	Arm 2	STOMP	Parent-reported pain interference score day 14	Day 14	Baseline: 296 Followup: 271	Baseline: NR Followup: Mean 8.63 (SD 8.39)	NR	Comparator: Arm 1 Mean difference: 0.57 (95% CI: -0.68 to 1.82), p=NR	NR

CI = confidence interval; N = sample size; NR = not reported; Ref = reference; SD = standard deviation; STOMP = Scenario-Tailored Opioid Messaging Program; VAS = Visual Analogue Scale

Evidence Table C-31. Number of pills per prescription (continuous data) of primary studies addressing effects of patient and family education or engagement related to use of prescribed or ordered opioids

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Delara, 2022[36]	Arm 1	Standard	Number of oxycodone pills prescribed at preoperative visit	NR	Baseline: 32 Followup: NR	Baseline: Median 30 (IQR 30.0, 30.0) Followup: NR	NR	Ref	NR
Delara, 2022[36]	Arm 2	Patient-directed	Number of oxycodone pills prescribed at preoperative visit	NR	Baseline: 33 Followup: NR	Baseline: Median 15 (IQR 12.0, 24.0) Followup: NR	NR	Comparator: Arm 1 p-value only: p< 0.001	NR
Stepan, 2021[35]	Arm 1	Control	Pills prescribed	NR	Baseline: 98 Followup: NR	Baseline: Mean 20 (Range 5-40) Followup: NR	NR	Ref	NR
Stepan, 2021[35]	Arm 2	Education	Pills prescribed	NR	Baseline: 93 Followup: NR	Baseline: Mean 15 (Range 5-50) Followup: NR	NR	Comparator: Arm 1 p-value only: p=NS	NR

IQR = interquartile range; N = sample size; NR = not reported; NS = not significant; Ref = reference

Evidence Table C-32. Total morphine milligram equivalents per prescription (continuous data) of primary studies addressing effects of patient and family education or engagement related to use of prescribed or ordered opioids

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Egan, 2020[33]	Arm 1	Control	Inpatient morphine milligram equivalents	NR	Baseline: 50 Followup: 46	Baseline: NR Followup: Mean 32.1 (SD 21.1)	NR	Ref	NR
Egan, 2020[33]	Arm 2	Interve ntion	Inpatient morphine milligram equivalents	NR	Baseline: 50 Followup: 39	Baseline: NR Followup: Mean 27.1 (SD 22.9)	NR	Comparator: Arm 1 p-value only: p=0.2	NR

N = sample size; NR = not reported; Ref = reference; SD = standard deviation

Evidence Table C-33. Overdose rates (categorical data) of primary studies addressing effects of clinical accountability interventions related to prescribed or ordered opioids

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Outcome Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Mingegshi, 2022[38]	Overall	Non-oversight	Opioid related serious adverse events such as opioid-related overdose or falls	Average 13 months	NR	NR	NR	Ref	No
Mingegshi, 2022[38]	Overall	Oversight	Opioid related serious adverse events such as opioid-related overdose or falls	Average 13 months	NR	NR	NR	Comparator: Arm 1 Hazards Ratio: 1.03 (95% CI: 0.97 to 1.08), p = NR	No

CI = confidence interval; N = sample size; NR = not reported; Ref = reference

Evidence Table C-34. Healthcare utilization outcome (categorical data) of primary studies addressing effects of multicomponent interventions

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Outcome Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Kasman et al, 2021[43]	Arm 1	Control	Clinic visit	30 days	54	NR (0)	Not reported	Comparator: Ref p-value only: p = 1	No
Kasman et al, 2021[43]	Arm 2	Intervention	Clinic visit	30 days	54	NR (0)	Not reported	Comparator: Arm 1 p-value only: p = 1	No
Kasman et al, 2021[43]	Arm 1	Control	ED visit	30 days	54	NR (3.7)	Not reported	Comparator: Ref p-value only: p = 1	No
Kasman et al, 2021[43]	Arm 2	Intervention	ED visit	30 days	54	NR (3.7)	Not reported	Comparator: Arm 1 p-value only: p = 1	No
Lamm, 2022[46]	Arm 1	Control	Calls to surgeon's office with pain within 30 days	30 days	58	10 (NR)	Not reported	Comparator: Ref p-value only: p = 0.022	No
Lamm, 2022[46]	Arm 2	Opioid Sparing	Calls to surgeon's office with pain within 30 days	30 days	42	10 (NR)	Not reported	Comparator: Arm 1 p-value only: p = 0.022	No
Lamm, 2022[46]	Arm 3	Zero-Opioid	Calls to Surgeon's Office with pain within 30 days	30 days	29	0 (NR)	Not reported	Comparator: Arm 1 p-value only: p = 0.022	No
Lamm, 2022[46]	Arm 1	Control	Pain medication refills within 30 days	30 days	58	3 (NR)	Not reported	Comparator: Ref p-value only: p = 0.218	No
Lamm, 2022[46]	Arm 2	Opioid Sparing	Pain medication refills within 30 days	30 days	42	4 (NR)	Not reported	Comparator: Arm 1 p-value only: p = 0.218	No

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Outcome Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Lamm, 2022[46]	Arm 3	Zero-Opioid	Pain medication refills within 30 days	30 days	29	0 (NR)	Not reported	Comparator: Arm 1 p-value only: p = 0.218	No
Vitzthum, 2022[44]	Arm 1	Pre-OSI	Pain-related ED visits, Q1	1 month before to 3 months	19382	NR	Not reported	Comparator: Arm 2 Cumulative incidence: Q1: 0.8, Q3: 0.3 (95% CI: Q1: 0.4 to 1, Q3: 0.1 to 0.6), p = 0.003	No
Vitzthum, 2022[44]	Arm 2	Post-OSI	Pain-related ED visits	1 month before to 3 months	22682	NR	Not reported	Comparator: Arm 1 Cumulative incidence: Q4: 1.8 (95% CI: 0.9 to 2.7), p = 0.003	No

CI = confidence interval; ED = emergency department; N = sample size; NR = not reported; OSI = Opioid Safety Initiative; Q1 = quarter 1; Q2 = quarter 2; Q3 = quarter 3; Q4=quarter 4; Ref = reference

Evidence Table C-35. Healthcare utilization outcome (continuous data) of primary studies addressing effects of multicomponent interventions

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Martinson, 2023[47]	Arm 1	PC-POP enrollees	ED visits	12 months	Baseline: 423 Followup: NR	Mean: 1.09	NR	Comparator: Arm 2 Mean: p=0.111	No
Martinson, 2023[47]	Arm 2	PC-POP non-enrollees	ED visits	12 months	Baseline: NR Followup: NR	Mean: 0.96	NR	Comparator: Arm 1 Mean: p=0.111	No
Martinson, 2023[47]	Arm 1	PC-POP enrollees	inpatient hospitalization	12 months	Baseline: 423 Followup: NR	Mean: 0.289	NR	Comparator: Arm 2 Mean: p=0.254	No
Martinson, 2023[47]	Arm 2	PC-POP non-enrollees	inpatient hospitalization	12 months	Baseline: NR Followup: NR	Mean: 0.334	NR	Comparator: Arm 1 Mean: p=0.254	NR
Neven, 2016[39]	Arm 1	Control	ED visits over 12 months	12 months	Baseline: NR Followup: NR	Baseline: Mean 15.46 (SD 5.6) Followup: Mean 8.49 (SD 7.02)	NR	Ref	NR
Neven, 2016[39]	Arm 2	Intervention	ED visits over 12 months	12 months	Baseline: NR Followup: NR	Baseline: Mean 16.67 (SD 6.76) Followup: Mean 5.59 (SD 4.65)	NR	Comparator: Arm 1 p-value only: p=0.003	NR
Neven, 2016[39]	Arm 1	Control	ED visit incidence (count per month)	12 months	Baseline: NR Followup: NR	NR	NR	Ref	NR
Neven, 2016[39]	Arm 2	Intervention	ED visit incidence (count per month)	12 months	Baseline: NR Followup: NR	NR	NR	Comparator: Arm 1 Odds Ratio: 0.663 (95% CI: 0.569 to 0.75), p=0.001	NR
Neven, 2016[39]	Arm 1	Control	ED visit (Yes/No per month)	12 months	Baseline: NR Followup: NR	NR	NR	Ref	NR

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Neven, 2016[39]	Arm 2	Intervention	ED visit (Yes/No per month)	12 months	Baseline: NR Followup: NR	NR	NR	Comparator: Arm 1 Incident Rate Ratio: 0.673 (95% CI: 0.538 to 0.841), p=0.001	stratification variables site (Boston vs Atlanta) and patient volume (1–2, 3–6, 7–11, and ≥12 patients)

CI = confidence interval; ED = emergency department; N = sample size; NR = not reported; OSI = Opioid Safety Initiative; PC-POP = Primary Care Pain Education and Opioid Monitoring Program; Ref = reference

Evidence Table C-36. Opioid refill request (categorical data) of primary studies addressing effects of multicomponent interventions

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Outcome Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Liebschutz, 2017[40]	Arm 1	Control	≥ 2 early refills (Baseline)	NR	399	94 (23.6)	NR	Ref	No
Liebschutz, 2017[40]	Arm 2	Intervention	≥ 2 early refills (Baseline)	NR	586	145 (24.7)	NR	Comparator: Arm 1 p-value only: p = 0.67	No
Liebschutz, 2017[40]	Arm 1	Control	≥ 2 early refills (Followup)	12 months	399	80 (20.1)	NR	Ref	No
Liebschutz, 2017[40]	Arm 2	Intervention	≥ 2 early refills (Followup)	12 months	586	121 (20.7)	NR	Comparator: Arm 1 Odds ratio: 1.1 (95% CI: 0.7 to 1.8), p = 0.82	No
Samet, 2021; Colasanti, 2022[41,42]	Arm 1	Control	≥1 early refill over 12 months	12 months	100	NR (30.4)	NR	Ref	No
Samet, 2021; Colasanti, 2022[41,42]	Arm 2	Intervention	≥1 early refill over 12 months	12 months	87	NR (21.6)	NR	Comparator: Arm 1 Odds ratio: 0.6 (95% CI: 0.26 to 1.15), p = 0.11	No

CI = confidence interval; N = sample size; NR = not reported; Ref = reference

Evidence Table C-37. Opioid refill request (continuous data) of studies addressing effects of multicomponent interventions

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Samet, 2021; Colasanti, 2022[41,42]	Arm 1	Control	Number of early refills over 12 months, mean (SD)	12 months	Baseline: 100 Followup: 100	Baseline: NR Followup: Mean 0.6 (SD 1.14)	NR	Ref	Stratification variables site (Boston vs Atlanta) and patient volume (1–2, 3–6, 7–11, and ≥12 patients)
Samet, 2021; Colasanti, 2022[41,42]	Arm 2	Intervention	No. of early refills over 12 months, mean (SD)	12 months	Baseline: 87 Followup: 87	Baseline: NR) Followup: Mean 0.46 (SD 1)	NR	Comparator: Arm 1 Odds Ratio: 0.64 (95% CI: 0.32 to 1.30), p=0.21	No

CI = confidence interval; N = sample size; NR = not reported; Ref = reference; SD = standard deviation

Evidence Table C-38. Pain intensity or distress outcome (categorical data) of studies addressing effects of multicomponent interventions

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Outcome Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Kasman et al, 2021[43]	Arm 1	Control	Phone call complaining of pain	30 days	54	NR (7.4)	Not reported	Comparator: Arm 2 p-value only: p = 1	No
Kasman et al, 2021[43]	Arm 2	Intervention	Phone call complaining of pain	30 days	54	NR (7.4)	Not reported	Comparator: Arm 1 p-value only: p = 1	No

CI = confidence interval; N = sample size; NR = not reported; Ref = reference

Evidence Table C-39. Pain intensity or distress outcome (continuous data) of primary studies addressing effects of multicomponent interventions

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Lamm, 2022[46]	Arm 1	Control	Pain Scores after discharge	NR	Baseline: 58 Followup: 58	Median: 3	NR	Comparator: Arm 2 Median: p=0.08	No
Lamm, 2022[46]	Arm 2	Opioid Sparing	Pain Scores after discharge	NR	Baseline: 42 Followup: 42	Median: 2	NR	Comparator: Arm 1 Median: p=0.08	No
Lamm, 2022[46]	Arm 3	Zero Opioid	Pain Scores after discharge	NR	Baseline: 29 Followup: 39	Median: 4	NR	Comparator: Arm 2 Median: p=0.08	NR
Morasco, 2022[45]	Arm 1	Education only	Pain intensity score	Baseline; 6 months; 12 months	Baseline: 136 Followup: 125; 123	Baseline: Mean 65.8 (SD 15.5) Followup: Mean 65.3; 62.1 (SD 17; 18)	NR	Ref	NR
Morasco, 2022[45]	Arm 2	ISOT	Pain intensity score	Baseline; 6 months; 12 months	Baseline: 150 Followup: 139; 135	Baseline: Mean 67 (SD 14.5) Followup: Mean 64.9; 64.9 (SD 16.3; 16.5)	NR	Comparator: Arm 1 p-value only: p=NS	NR
Morasco, 2022[45]	Arm 1	Education only	Pain interference score	Baseline; 6 months; 12 months	Baseline: 136 Followup: 125; 123	Baseline: Mean 54 (NR 28) Followup: Mean 53.3; 48.2 (SD 28.9; 28.9)	NR	Ref	NR
Morasco, 2022[45]	Arm 2	ISOT	Pain interference score	Baseline; 6 months; 12 months	Baseline: 150 Followup: 139; 135	Baseline: Mean 58.7 (NR 28.1) Followup: Mean 55.6; 53.4 (SD 28.6; 28.7)	NR	Comparator: Arm 1 p-value only: p=NS	Stratification variables site (Boston vs Atlanta) and patient volume (1–2, 3–6, 7–11, and ≥12 patients)

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Samet, 2021; Colasanti, 2022[41,42]	Arm 1	Control	Pain severity (BPI), mean (SD)	NR	Baseline: 100 Followup: 100	Baseline: NR Followup: Mean 5.76 (SD 2.87)	NR	Ref	stratification variables site (Boston vs Atlanta) and patient volume (1–2, 3–6, 7–11, and ≥12 patients)
Samet, 2021; Colasanti, 2022[41,42]	Arm 2	Intervention	Pain severity (BPI), mean (SD)	NR	Baseline: 87 Followup: 87	Baseline: NR Followup: Mean 6.3 (SD 2.87)	NR	Comparator: Arm 1 Odds Ratio: 0.1 (95% CI: -1.56 to 1.75), p=0.91	stratification variables site (Boston vs Atlanta) and patient volume (1–2, 3–6, 7–11, and ≥12 patients)
Samet, 2021; Colasanti, 2022[41,42]	Arm 1	Control	Pain interference (BPI), mean (SD)	NR	Baseline: 100 Followup: 100	Baseline: NR Followup: Mean 4.99 (SD 3.58)	NR	Ref	stratification variables site (Boston vs Atlanta) and patient volume (1–2, 3–6, 7–11, and ≥12 patients)
Samet, 2021; Colasanti, 2022[41,42]	Arm 2	Intervention	Pain interference (BPI), mean (SD)	NR	Baseline: 87 Followup: 87	Baseline: NR Followup: Mean 5.7 (SD 2.98)	NR	Comparator: Arm 1 Odds Ratio: 0.3 (95% CI: -1.34 to 1.95), p=0.72	No

BPI = Brief Pain Inventory; CI = confidence interval; N = sample size; NR = not reported; NS = not significant; Ref = reference; SD = standard deviation

Evidence Table C-40. Patient satisfaction outcome (categorical data) of primary studies addressing effects of multicomponent interventions

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Outcome events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Samet, 2021; Colasanti, 2022[41,42]	Arm 1	Control	Patient satisfied with the way the clinic manages pain (75th percentile, range 1–10)	12 months	48	27 (56.3)	NR	Ref	No
Samet, 2021; Colasanti, 2022[41,42]	Arm 2	Intervention	Patient satisfaction with the way the clinic manages pain (75th percentile, range 1–10)	12 months	57	31 (54.4)	NR	Comparator: Arm 1 Odds ratio: 1.17 (95% CI: 0.5 to 2.76), p = 0.72	No

CI = confidence interval; N = sample size; NR = not reported; Ref = reference

Evidence Table C-41. Patient satisfaction outcome (continuous data) of primary studies addressing effects of multicomponent interventions

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Lamm, 2022[46]	Arm 1	Control	Satisfaction scores after discharge	NR	Baseline: 58 Followup: 58	Median: 10	NR	Comparator: Arm 1 Median: p=0.8302	No
Lamm, 2022[46]	Arm 2	Opioid Sparing	Satisfaction scores after discharge	NR	Baseline: 42 Followup: 42	Median: 10	NR	Comparator: Arm 2 Median: p=0.8302	No
Lamm, 2022[46]	Arm 3	Zero Opioid	Satisfaction scores after discharge	NR	Baseline: 29 Followup: 39	Median: 10	NR	Comparator: Arm 1 Median: p=0.8302	NR

N = sample size; NR = not reported; Ref = reference

Evidence Table C-42. Rates of opioid prescribing outcome (categorical data) of primary studies addressing effects of multicomponent interventions

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Outcome Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Kasman et al, 2021[43]	Arm 1	Control	Opioid prescription at discharge	NR	54	NR (88.9)	NR	Comparator: Arm 2 p-value only: p <0.001	No
Kasman et al, 2021[43]	Arm 2	Intervention	Opioid prescription at discharge	NR	54	NR (3.7)	NR	Comparator: Arm 1 p-value only: p <0.001	No
Kasman et al, 2021[43]	Arm 1	Control	Opioid prescription at post-discharge	30 days	54	NR (1.9)	NR	Comparator: Arm 2 p-value only: p = 0.56	No
Kasman et al, 2021[43]	Arm 2	Intervention	Opioid prescription at post-discharge	30 days	54	NR (3.7)	NR	Comparator: Arm 1 p-value only: p = 0.56	No
Liebschutz, 2017[40]	Arm 1	Control	Discontinuation of opioid prescription (Followup)	12 months	399	67 (16.8)	NR	Ref	No
Liebschutz, 2017[40]	Arm 2	Intervention	Discontinuation of opioid prescription (Followup)	12 months	586	125 (21.3)	NR	Comparator: Arm 1 Odds ratio: 1.5 (95% CI: 1 to 2.1), p = 0.08	No

CI = confidence interval; N = sample size; NR = not reported; Ref = reference

Evidence Table C-43. Rates of opioid prescribing outcome (continuous data) of primary studies addressing effects of multicomponent interventions

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Neven, 2016[39]	Arm 1	Control	Opioid prescriptions from the ED over 12 months	Over 12 months	Baseline: 76 Followup: 76	Baseline: Mean 3.65 (SD 3.69) Followup: Mean 1.44 (SD 2.05)	NR	Ref	NR
Neven, 2016[39]	Arm 2	Intervention	Opioid prescriptions from the ED over 12 months	Over 12 months	Baseline: 79 Followup: 79	Baseline: Mean 3.97 (SD 3.97) Followup: Mean 0.28 (SD 0.74)	NR	Comparator: Arm 1 p-value only: p< 0.0001	NR
Neven, 2016[39]	Arm 1	Control	Opioid incidence in ED (count per month)	Over 12 months	Baseline: 76 Followup: 76	NR	NR	Ref	NR
Neven, 2016[39]	Arm 2	Intervention	Opioid incidence in ED (count per month)	Over 12 months	Baseline: 79 Followup: 79	NR	NR	Comparator: Arm 1 Odds Ratio: 0.208 (95% CI: 0.122 to 0.353), p=0.586	NR
Neven, 2016[39]	Arm 1	Control	Opioid in ED (yes/no)	Over 12 months	Baseline: 76 Followup: 76	NR	NR	Ref	NR
Neven, 2016[39]	Arm 2	Intervention	Opioid in ED (yes/no)	Over 12 months	Baseline: 79 Followup: 79	NR	NR	Comparator: Arm 1 Incident Rate Ratio: 0.198 (95% CI: 0.12 to 0.325), p=0.49	No
Vitzthum, 2022[44]	Arm 1	Pre-OSI	Incidence of new opioid prescription	1 month before to 3 months	Baseline: 19382 Followup: NR	Median rate: 24.1	NR	Comparator: Arm 2 Median rate: p<0.001	No

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Vitzthum, 2022[44]	Arm 2	Post-OSI	Incidence of new opioid prescription	1 month before to 3 months	Baseline: 22682 Followup: NR	Median rate: (-)3.5	NR	Comparator: Arm 1 Median rate: p<0.001	No

CI = confidence interval; ED = emergency department; N = sample size; NR = not reported; OSI = Opioid Safety Initiative

Evidence Table C-44. Other referrals relevant to paint management outcomes (continuous data) of primary studies addressing effects of multicomponent interventions

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N	Results	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Martinson, 2023[47]	Arm 1	PC-POP enrollees	Number of cognitive-behavioral therapy for chronic pain consuls	12 months	Baseline: 423 Followup: NR	Mean: 0.164	NR	Comparator: Arm 2 Mean: p<0.001	No
Martinson, 2023[47]	Arm 2	PC-POP non-enrollees	Number of cognitive-behavioral therapy for chronic pain consults	12 months	Baseline: NR Followup: NR	Mean: 0.019	NR	Comparator: Arm 1 Mean: p<0.001	No
Martinson, 2023[47]	Arm 1	PC-POP enrollees	Number of whole health services consults	12 months	Baseline: 423 Followup: NR	Mean: 0.384	NR	Comparator: Arm 2 Mean: p<0.001	No
Martinson, 2023[47]	Arm 2	PC-POP non-enrollees	Number of whole health services consults	12 months	Baseline: NR Followup: NR	Mean: 0.035	NR	Comparator: Arm 1 Mean: p<0.001	No
Martinson, 2023[47]	Arm 1	PC-POP enrollees	Number of living with chronic conditions consults	12 months	Baseline: 423 Followup: NR	Mean: 0.057	NR	Comparator: Arm 2 Mean: p<0.001	No
Martinson, 2023[47]	Arm 2	PC-POP non-enrollees	Number of living with chronic conditions consults	12 months	Baseline: NR Followup: NR	Mean: 0.003	NR	Comparator: Arm 1 Mean: p<0.001	No
Martinson, 2023[47]	Arm 1	PC-POP enrollees	Number of mindfulness center consults	12 months	Baseline: 423 Followup: NR	Mean: 0.028	NR	Comparator: Arm 2 Mean: p=0.132	No
Martinson, 2023[47]	Arm 2	PC-POP non-enrollees	Number of mindfulness center consults	12 months	Baseline: NR Followup: NR	Mean: 0.013	NR	Comparator: Arm 1 Mean: p=0.132	No
Martinson, 2023[47]	Arm 1	PC-POP enrollees	Number of Trauma sensitivity yoga consults	12 months	Baseline: 423 Followup: NR	Mean: 0.073	NR	Comparator: Arm 2 Mean: p<0.001	No
Martinson, 2023[47]	Arm 2	PC-POP non-enrollees	Number of Trauma sensitivity yoga consults	12 months	Baseline: NR Followup: NR	Mean: 0	NR	Comparator: Arm 1 Mean: p<0.001	No

N = sample size; NR = not reported; PC-POP = Primary Care Pain Education and Opioid Monitoring Program

Evidence Table C-45. Risk assessment outcomes (categorical data) of primary studies addressing effects of multicomponent interventions

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Outcome Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Samet, 2021; Colasanti, 2022[41,42]	Arm 1	Control	Provider routinely consulted prescription monitoring program	12 months	100	NR (45)	NR	Ref	No
Samet, 2021; Colasanti, 2022[41,42]	Arm 2	Interventio n	Provider routinely consulted prescription monitoring program	12 months	87	NR (71.4)	NR	Comparator: Arm 1 Odds ratio: 3.85 (95% CI: 0.99 to 14.93), p = 0.05	No

CI = confidence interval; N = sample size; NR = not reported; Ref = reference

Evidence Table C-46. Total morphine milligram equivalents per prescription (continuous data) of primary studies addressing effects of multicomponent interventions

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N	Results	Between Arm Comparison	Adjusted Factors
Kasman et al, 2021[43]	Arm 1	Control	0	NR	Baseline: 54 Followup: NR	Mean: 110.55	Comparator: Arm 2 Mean: p<0.001	No
Kasman et al, 2021[43]	Arm 2	Intervention	0	NR	Baseline: 54 Followup: NR	Mean: 12.03	Comparator: Arm 1 Mean: p<0.002	No
Kasman et al, 2021[43]	Arm 1	Control	0	NR	Baseline: 54 Followup: NR	Mean: 1.85	Comparator: Arm 2 Mean: p=0.92	No
Kasman et al, 2021[43]	Arm 2	Intervention	0	NR	Baseline: 54 Followup: NR	Mean: 2.11	Comparator: Arm 1 Mean: p=0.92	No
Lamm, 2022[46]	Arm 1	Control	MME in PACU	NR	Baseline: 58 Followup: 58	Median: 15	Comparator: Arm 2 Median: p=0.3368	No
Lamm, 2022[46]	Arm 2	Opioid Sparing	MME in PACU	NR	Baseline: 42 Followup: 42	Median: 7.5	Comparator: Arm 1 Median: p=0.3368	No
Lamm, 2022[46]	Arm 3	Zero Opioid	MME in PACU	NR	Baseline: 29 Followup: 39	Median: 15	Comparator: Arm 2 Median: p=0.3368	No
Lamm, 2022[46]	Arm 1	Control	MME after discharge	NR	Baseline: 58 Followup: 58	Median: 46	Comparator: Arm 1 Median: p=0.0001	No
Lamm, 2022[46]	Arm 2	Opioid Sparing	MME after discharge	NR	Baseline: 42 Followup: 42	Median: 15	Comparator: Arm 2 Median: p=0.0001	No

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N	Results	Between Arm Comparison	Adjusted Factors
Lamm, 2022[46]	Arm 3	Zero Opioid	MME after discharge	NR	Baseline: 29 Followup: 39	Median: 0	Comparator: Arm 1 Median: p=0.0001	Drug use diagnosis, mental health problems, English-speaking, and baseline levels of outcome measures
Liebschutz, 2017[40]	Arm 1	Control	MEDD	12 months	Baseline: 399 Followup: 399	Baseline: Mean 62.3 (SD 75.6) Followup: Mean 67.3 (SD 80.4)	Ref	Drug use diagnosis, mental health problems, English-speaking, and baseline levels of outcome measures
Liebschutz, 2017[40]	Arm 2	Intervention	MEDD	12 months	Baseline: 586 Followup: 586	Baseline: Mean 61.1 (SD 84.9) Followup: Mean 60.8 (SD 93.7)	Comparator: Arm 1 Beta coefficient: -6.8 (SE 1.6), p=0.31	No
Martinson, 2023[47]	Arm 1	PC-POP enrollees	MEDD dose	12	Baseline: 423 Followup: NR	Mean: 40.96	Comparator: Arm 2 Mean: p=0.284	No
Martinson, 2023[47]	Arm 2	PC-POP non-enrollees	MEDD dose	12	Baseline: NR Followup: NR	Mean: 35.44	Comparator: Arm 1 Mean: p=0.284	NR

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N	Results	Between Arm Comparison	Adjusted Factors
Morasco, 2022[45]	Arm 1	Education only	Prescription opioid dose in mg morphine equivalents at final visit	NR	Baseline: NR Followup: NR	Baseline: NR Followup: Mean 33.6 (SD 42.2)	Ref	NR
Morasco, 2022[45]	Arm 2	ISOT	Prescription opioid dose in mg morphine equivalents at final visit	NR	Baseline: NR Followup: NR	Baseline: NR Followup: Mean 34.4 (SD 34.8)	Comparator: Arm 1 p-value only: p=0.57	No

CI = confidence interval; MEDD = morphine equivalent daily dose; mg=milligram; MME = morphine milligram equivalent; N = sample size; NR=not reported; PACU = post-anesthesia care unit; PC-POP = Primary Care Pain Education and Opioid Monitoring Program

Evidence Table C-47. Treatment agreement use (categorical data) of studies addressing effects of multicomponent interventions

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Outcome Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Liebschutz, 2017[40]	Arm 1	Control	Guideline-concordant care (agreement plus UDT) (Baseline)	NR	399	168 (42.1)	NR	Ref	No
Liebschutz, 2017[40]	Arm 2	Intervention	Guideline-concordant care (agreement plus UDT) (Baseline)	NR	586	241 (41.1)	NR	Comparator: Arm 1 p-value only: p = 0.76	No
Liebschutz, 2017[40]	Arm 1	Control	Guideline-concordant care (agreement plus UDT) (Followup)	12 months	399	151 (37.8)	NR	Ref	No
Liebschutz, 2017[40]	Arm 2	Intervention	Guideline-concordant care (agreement plus UDT) (Followup)	12 months	586	386 (65.9)	NR	Comparator: Arm 1 Odds ratio: 6 (95% CI: 3.6 to 10.2), p < 0.001	No
Liebschutz, 2017[40]	Arm 1	Control	Patient ever signed an agreement (Baseline)	NR	399	233 (58.4)	NR	Ref	No
Liebschutz, 2017[40]	Arm 2	Intervention	Patient ever signed an agreement (Baseline)	NR	586	376 (64.2)	NR	Comparator: Arm 1 p-value only: p = 0.07	No
Liebschutz, 2017[40]	Arm 1	Control	Patient ever signed an agreement (Followup)	12 months	399	243 (60.9)	NR	Ref	No
Liebschutz, 2017[40]	Arm 2	Intervention	Patient ever signed an agreement (Followup)	12 months	586	489 (83.5)	NR	Comparator: Arm 1 p-value only: p < 0.001	No
Liebschutz, 2017[40]	Arm 1	Control	No baseline agreement (Baseline)	NR	166	166 (100)	NR	Ref	No

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Outcome Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Liebschutz, 2017[40]	Arm 2	Intervention	No baseline agreement (Baseline)	NR	210	210 (100)	NR	Comparator: Arm 1 p-value only: p = NA	No
Liebschutz, 2017[40]	Arm 1	Control	No baseline agreement (Followup)	12 months	166	10 (6)	NR	Ref	No
Liebschutz, 2017[40]	Arm 2	Intervention	No baseline agreement (Followup)	12 months	210	133 (53.8)	NR	Comparator: Arm 1 Odds ratio: 11.9 (95% CI: 4.4 to 32.2), p < 0.001	No
Samet, 2021; Colasanti, 2022[41,42]	Arm 1	Control	Opioid treatment agreement	12 months	100	NR (12.8)	NR	Ref	No
Samet, 2021; Colasanti, 2022[41,42]	Arm 2	Intervention	Opioid treatment agreement	12 months	87	NR (75.6)	NR	Comparator: Arm 1 Odds ratio: 61.5 (95% CI: 15.30 to 247.20), p <0.0001	No

CI = confidence interval; N = sample size; NR = not reported; Ref = reference; UDT = urine drug test

Evidence Table C-48. Urine drug screen ordering or administration (categorical data) of primary studies addressing effects of multicomponent interventions

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N at Analysis	Patients With Events, n (%)	Within Arm Comparison	Between Arm Comparison	Adjusted Factors
Liebschutz, 2017[40]	Arm 1	Control	UDT (once in past 12 months) (Baseline)	NR	399	259 (64.9)	NR	Ref	No
Liebschutz, 2017[40]	Arm 2	Intervention	UDT (once in past 12 months) (Baseline)	NR	586	348 (59.4)	NR	Comparator: Arm 1 p-value only: p < 0.08	No
Liebschutz, 2017[40]	Arm 1	Control	UDT (once in past 12 months) (Followup)	12 months	399	231 (57.9)	NR	Ref	No
Liebschutz, 2017[40]	Arm 2	Intervention	UDT (once in past 12 months) (Followup)	12 months	586	437 (74.6)	NR	Comparator: Arm 1 Odds ratio: 3 (95% CI: 1.8 to 5), p < 0.001	No
Samet, 2021; Colasanti, 2022[41,42]	Arm 1	Control	≥2 urine drug tests over 12 months	12 months	100	NR (19.9)	NR	Ref	No
Samet, 2021; Colasanti, 2022[41,42]	Arm 2	Intervention	≥2 urine drug tests over 12 months	12 months	87	NR (71)	NR	Comparator: Arm 1 Odds ratio: 13.38 (95% CI: 5.85 to 30.60), p <0.0001	No

CI = confidence interval; N = sample size; NR = not reported; Ref = reference; UDT = urine drug test

Evidence Table C-49. Urine drug screen ordering or administration (categorical data) of primary studies addressing effects of multicomponent interventions

Author, Year	Arm	Arm Name	Outcome Definition	Time Point at Analysis	N	Results	Between Arm Comparison	Adjusted Factors
Martinson, 2023[47]	Arm 1	PC-POP enrollees	Urinary Drug Test	12 months	Baseline: 423 Followup: NR	Mean: 2.32	Comparator: Arm 2 Mean: p=0.461	No
Martinson, 2023[47]	Arm 2	PC-POP non-enrollees	Urinary Drug Test	12 months	Baseline: NR Followup: NR	Mean: 0.95	Comparator: Arm 1 Mean: p=0.461	No
Martinson, 2023[47]	Arm 1	PC-POP enrollees	Patient Drug Monitoring Program	12 months	Baseline: 423 Followup: NR	Mean: 2.382	Comparator: Arm 2 Mean: p<0.001	No
Martinson, 2023[47]	Arm 2	PC-POP non-enrollees	Patient Drug Monitoring Program	12 months	Baseline: NR Followup: NR	Mean: 2.219	Comparator: Arm 1 Mean: p=0.428	No

CI = confidence interval; N = sample size; NR = not reported; PC-POP = Primary Care Pain Education and Opioid Monitoring Program; Ref = reference

Evidence Table C-50. Characteristics and reported outcomes of identified pre-post studies addressing harms, effectiveness and unintended effects of opioid stewardship practices

Author, Year	Intervention	Setting	Outcomes
Anderson, 2016[75]	Education on pain care, new protocols for pain assessment and management, implementation of an opioid management dashboard, telehealth consultations, and enhanced onsite specialty resources	Multisite federally qualified health center	Use of opioid treatment agreements; urine drug screens; pain score; pain treatment; pain followup; referrals; opioid prescribing
Angelo, 2019[76]	In-service training for surgical staff and distribution of standardized guidelines	Public hospital	Opioid prescriptions; emergency room visits
Arthur, 2022[77]	Compassionate High-Alert Team (CHAT) intervention	Ambulatory	Pain score; Morphine equivalent daily dose
Asmaro, 2021[78]	Provider education	Surgery (craniotomy)	Quantity of opioids prescribed; refill rates; pain
Awadallah, 2022[79]	Interprofessional safe prescribing committee, policy, and protocol	Not specified	Total MME prescribed; pain
Baker, 2022[80]	Tiered guidelines for discharge opioid prescription	Ambulatory	Oral morphine equivalents (OMEs) prescribed at discharge; 30-day refill rate; Prescriptions within OME guidelines
Banik, 2021[81]	Preoperative counseling, multimodality pain management, and multidisciplinary collaboration	Tertiary academic hospital	Quantity of opioids prescribed during hospitalization; at discharge; and in refills
Beauchamp, 2022[82]	Providing feedback on the average morphine milligram equivalents (MMED) and opioid utilization by patients	Post-surgery	Total MMED; total number of pills prescribed; refill rates; readmissions
Berkley, 2023[83]	Pain management guideline	Post-surgery (kidney transplant)	Refill requests; pain; multimodal analgesic agents; number of opioid tablets prescribed
Boitana,2020[84]	Post-surgical restrictive opioid prescribing algorithm (ROPA); Patients were educated preoperatively about pain management goals, the ROPA, and opioid disposal.	Inpatient/ambulatory	Average number of opioid pills prescribed; morphine milligram equivalents (MME); opioid refill within 30 days; total number of pills prescribed annually; satisfaction
Brescia, 2021[85]	Evidence-based prescribing guidelines	Inpatient	Patient-reported outcomes; prescription size; Pain levels; refills; opioid prescribing
Brown, 2021[86]	Leveraged continuous quality improvement infrastructure to implement opioid prescribing guidelines	Inpatient/ambulatory	Prescription size; opioid consumption; patient-reported outcomes
Bryl, 2021[87]	Plan-Do-Study-Act cycles: guidelines and education, electronic medical record optimization, and provider-specific feedback.	Ambulatory	Opioid doses prescribed; opioid doses per prescription calls and return visits for poor pain control;
Bui, 2020[88]	Pharmacist-led opioid de-escalation service	Ambulatory	OME; pain intensity scores; opioid-related side effects

Author, Year	Intervention	Setting	Outcomes
Cairo, 2019[89]	Educational interventions included staff education, institution of opioid standardization protocol, and distribution of educational materials to families	Ambulatory	Prescription for opioids at time of discharge; pain control; emergency department visits or phone calls for poorly controlled pain
Chamber, 2022[90]	Orthopedic Trauma Association (OTA) pain management guidelines	Ambulatory	Prescription size; pain control; refills; morphine equivalent dose (MED); adherence to guidelines;
Chen, 2019[91]	Provider focused education	Not specified	Prescribing volumes; number of prescribers; ED visits
Chen, 2019[92]	The Opioid Safety Initiative (not specified)	Veterans' Health Administration medical centers	Pain scores; proportion with opioid prescriptions
Chiu, 2019[93]	Provider education, change in default electronic medication order entry system, distribution of guideline cards	Surgery department	Amount of opioids prescribed*; refill rates
Choo, 2019[94]	Medical providers received reports every 2 months	Not specified	Amount of opioids prescribed*; refill rates
Chua, 2022[95]	Recommended dosing quantities	Emergency department	Number of opioids prescribed; second opioid prescription rate; ED visits; pain related telephone calls or orthopedic visits
Ciampa, 2023[96]	Prescribing guidelines: shared decision making and patient education	Surgical department	Number of pills prescribed; unused pills; number of excess pills returned to pharmacy; patient satisfaction
Colloca, 2022[97]	Educational intervention to modify perceptions of opioid	Inpatient	Morphine Milligram Equivalents, patient satisfaction
Corday, 2022[98]	Standardized opioid-sparing analgesic protocol	Post-surgery (hospital-based tonsillectomy)	Number of doses prescribed; morphine equivalents/kg/dose; returns to emergency departments or hospital readmissions; Protocol adherence; Opioid quantities per prescription; incidence of returns to the system
DeUgarte, 2023[99]	(1) Promoting and optimizing use of nonopioids (e.g., acetaminophen and nonsteroidal anti-inflammatory medications), (2) discouraging combination drugs to maximize acetaminophen dosing, (3) removing formulary restrictions on oxycodone, (4) updating pain management order sets in the electronic medical record (EMR), and (5) auditing adherence with feedback to surgical leadership.	Inpatient/ambulatory	Perioperative morphine milligram equivalents; Number of opioid pills prescribed; Morphine milligram equivalents prescribed; Prescribed less than recommended pills/procedures audited; Return to emergency department within days
Dualeh, 2021[100]	Opioid restrictive post-operative pain management protocol	Inpatient/ambulatory	Oral morphine milligram equivalence (OME); opioid tablets prescribed at discharge; amount of opioid prescribed* within first 30 days; number of patient calls for pain complaint; opioid prescription in electronic medical record at 90 days and 1 year

Author, Year	Intervention	Setting	Outcomes
Embty, 2020[101]	Quality improvement project sought to increase use of evidence-based multimodal pain management strategies	Not specified	Number of patients receiving 30-day supplies of opioids
Featherall, 2022[102]	Multidisciplinary, perioperative pain management program	Veterans Affairs Medical Center	Opioid use at 90 days; post-operative outcome scores; time to opioid cessation; and median opioid tablets consumed at 90 days
Findlay, 2021[103]	Prescribing guideline	Urology department	Quantity of opioids prescribed; refill rates
Gerges, 2022[104]	Policy interventions	Tertiary academic medical center	Medication; dose; morphine milliequivalents; post-discharge opioid prescriptions; ED visits; post-operative phone calls
Grabski, 2021[105]	Standardizing post-surgical sign-out between the surgical, anesthesia and NICU teams and a series of education seminars	Neonatal intensive care unit	Post-operative opioid use; pain scores; safety profiles; incubation length
Gudmundsdottir, 2022[106]	Opioid prescription guidelines	General surgery	Prescriptions falling within recommendations; refill rates; opioid dose (MME); patient satisfaction
Guptak, 2020[107]	Intervention aimed to inform and educate providers about the CDC's guidelines and to improve adherence	Ambulatory	Opioid prescription rate; patient satisfaction scores
Hartford, 2019[108]	Outpatient Procedure (STOP) Narcotics	Ambulatory	Postoperative pain; quality of pain control; median oral morphine equivalents (MME)
Hartford, 2019[109]	Outpatient Procedure (STOP) Narcotics	Ambulatory	Pain during the first 7 postoperative days; median oral morphine equivalents prescribed; Prescription renewals
Hite, 2021[110]	Implementation of standardized prescribing, voluntary and anonymous survey analysis, and preoperative education regarding risks of opioids, charcoal disposal bag distribution, and followup survey to assess use and use of intervention.	Inpatient/ambulatory	Narcotic prescriptions; postoperative pain control satisfaction score
Horton, 2020[111]	Standardized EMR order set	Pediatric post-tonsillectomy	Quantity of opioids prescribed; pain; postoperative hemorrhage; ED presentation; readmissions
Huepenbecker, 2021[112]	Tiered opioid prescribing algorithm	Inpatient/ambulatory	Morphine equivalent dose; opioid refills; 30-day readmission rate; patient-reported pain
Jamieson, 2019[113]	Opioid calculator and pain plan	Ambulatory surgery center	Number of pills prescribed; opioid consumption; patient satisfaction; refill rates
Jung, 2021[114]	Opioid sparing protocol	Inpatient	Opioids administered during hospitalization; amount of opioids* prescribed at discharge (MME); pain scores
Kaafarani, 2019[115]	Multispecialty multidisciplinary: guidelines, provider education	Surgical units	Prescribing OME dosage

Author, Year	Intervention	Setting	Outcomes
Kaimakliotis, 2021[116]	Educational intervention providing analgesic decision support to staff	Internal medicine and emergency medicine	Reduction in aggregate inpatient opioid use; new opioid prescriptions; hospital length of stay; readmission rates; pain scores
Kelly-Quon, 2022[117]	Quality Improvement methodology	Ambulatory	Opioid prescribing; 30-day emergency room visits; postintervention pain management satisfaction scores
Kemp, 2021[118]	30-minute lecture for general surgery residents that discussed prescribing guidelines and multimodal analgesia	Inpatient	Opioid volumes (normalized to oral morphine equivalents, OME); opioid type; nonopioid pain medications; refills requested
Krauss, 2021[119]	Departmental postoperative prescribing guidelines	Inpatient/ambulatory	Prescriptions in morphine milliequivalents; refills within 30 days; guideline compliance; opioid prescription rate
Krebsbacj, 2022[120]	Trauma discharge opioid bundle	Inpatient	Total morphine milligram equivalents prescribed; outpatient refills within fourteen days
Kshirsagar, 2021[121]	Standardizing opioid prescription practice, encouraging multimodal analgesia	Post-surgery (otolaryngology)	Pain; patients receiving opioids; number of opioid doses
Lamm, 2023[122]	Opioid reduction toolkit (not specified)	Post-surgery	Median dose prescribed; MME's consumed; refill rates; patient awareness of safe disposal
Lavingia, 2021[123]	Provider education, changes in EMR, discharge resources, process standardization	Pediatric emergency department	Opioid prescription rates; opioid discharge instructions; enrollment in PDMP; return visits
Lee, 2021[124]	Patient education intervention	Post-pediatric umbilical hernia surgery	Prescriptions; prescription fills; patient medication use; pain control; adverse events
Lindros, 2023[125]	Prescribing guidelines	Surgery department (ventral hernia repair)	Patient-reported outcomes (including pain); refill rates; length of stay
Margolis, 2020[126]	Preoperative counseling, standardization of perioperative analgesia, and a postoperative opioid prescribing algorithm	Tertiary medical center	Percent patients discharged with opioids; number of opioid tablets prescribed; refill rates or new prescription; pain
McGee, 2020[127]	Procedure-specific prescribing guidelines and trainee education	Inpatient/ambulatory	Postoperative opioid prescribing, opioid refills, and emergency department (ED) visits within 21 days after surgery
Mears, 2019[128]	Department prescribing policy: recommendations of number of tablets per procedure, patient education	Surgery department	Number of opioids prescribed; number of MMEs prescribed; refill rates
Meyer, 2021[129]	Institutional prescribing guideline	Inpatient	Opioid prescribing; Days from discharge to followup; any complication; any readmission refills
Mittal, 2020[130]	Quality improvement initiative aimed to reduce post-operative opioids for pain management	Ambulatory	Opioid prescription rate; nonopioid analgesia; office visits within 5 days; overall ED visits; ED visits for pain
Mou, 2022[131]	Electronic health record order set containing prepopulated tablet quantities tailored to surgical procedures based on published guidelines	Inpatient/ambulatory	Mean morphine milligram equivalent; emergency department visits for pain-related issues; opioid refill rates
Nguyen, 2020[132]	Education to surgical residents	Tertiary care center	MME prescribed; pain; ED visits; readmissions due to pain

Author, Year	Intervention	Setting	Outcomes
Nouree, 2021[133]	Presentations of opioid prescribing at physician level, prescription guidelines, PMP registration, patient education	Private orthopedic practice	Number of opioid pills; dose (morphine equivalent units); pain score; patient satisfaction
Olsen, 2020[134]	Cease routine provision of opioid prescribing at discharge	Obstetrics and gynecology	Proportion of patients provided with opioid prescription; patient encounters due to pain
Padilla, 2019[135]	Opioid-sparing pain management pilot	Inpatient	Inpatient morphine milligram equivalents
Parker, 2023[136]	Postoperative 7-day opioid wean and designed a dashboard to track the information gathered	Inpatient	Prescription for 30 pills or less; hospitalizations; morphine milligram equivalents per day; quantity prescribed; opioid refill requests; return visit rates
Peterman, 2020[137]	Standardized prescribing protocol	Post-surgery (ventral hernia repair)	Total MME prescribed; refill rates
Pierce, 2022[138]	A vendor-developed provider-targeted Clinical decision support systems	Ambulatory	Count of opioid prescriptions, morphine milligram equivalents per prescription, counts of opioids with concurrent benzodiazepines, and counts of short-acting opioids in opioid-naïve patients; rates of encounters for opioid abuse and dependence and rates of encounters for opioid poisoning and overdose; rates of provision of naloxone and documentation of opioid treatment agreements
Piper, 2020[139]	Educational intervention: The intervention highlighted the importance of opioid stewardship, demonstrated practice variation, provided prescribing guidelines, encouraged nonopioid analgesics, and encouraged limiting doses/strength if opioids were prescribed	Inpatient/ambulatory	Number of doses prescribed; morphine equivalents/kg/dose; return to emergency departments or hospital readmissions
Price-Hayewood, 2020[140]	Electronic medical record clinical decision support	Primary care	Change in the average MEDD; rates of opioid risk mitigation; hospitalization; emergency department use
Pruitt, 2020[141]	Prescription guidelines	23-hospital system surgical departments	Prescription of opioids; number of pills consumed
Reisener, 2021[142]	Opioid stewardship program (not specified)	Orthopedic surgery specialty hospital	In-hospital opioid consumption; pain scores; length of stay; side effects; discharge prescribing
Rennert, 2023[143]	Nonopioid medication during surgery, decreasing available opioid dosage; standardizing of opioid inpatient practices, limiting post-surgery opioid supply	A large healthcare system	Discharge pain; MME in first prescription post-surgery; refill rates
Rizk, 2022[144]	Patient education flyer, electronic health record order sets with multimodal analgesia regimens, and provider education	Academic medical center	New opioid discharge prescriptions; opioid discharge prescriptions that exceeded 112.5 MME; five days of therapy
Rohan, 2020[145]	Education on opioids and a multimodal pain regimen	Post-surgery	Average daily MME; opioid utilization
Seu, 2022[146]	Multimodal perioperative pain management regimen	Bariatric surgery	Inpatient opioid use; length of stay; nonopioid analgesic use

Author, Year	Intervention	Setting	Outcomes
Slater, 2022[147]	Patient education intervention	Post-surgery	Medication refills; opioid prescribing rates; emergency department returns or readmissions
Smith, 2022[148]	Limit the use of the intravenous (IV) push route for opioids	General medicine floor units	Pain score; hospital length of stay; patient satisfaction; percent exposed to opioid administration; transfer to ICU; incidence of naloxone administration
Starr, 2020[149]	Prescribing guidelines	Post-ophthalmic surgery	Opioid prescription frequency; quantity of opioids prescribed; refill rates
Thal, 2022[150]	Prescription protocol	Post-surgery otolaryngology	Change in amount of opioids* prescribed; unplanned contact due to pain; refill rates
Tyson, 2023[151]	Guideline to standardize opioid prescribing	Inpatient	Total morphine milligram equivalents and maximum morphine milligram equivalents per day; patients prescribed morphine milligram equivalents per day at discharge; patients prescribed morphine milligram equivalents per day; frequency of refill requests (P =.105) or refill prescriptions (P =.099) after discharge.
Vilkins, 2019[152]	A visual decision aid, patients received uniform education regarding postoperative pain management	Inpatient/ambulatory	Total opioids prescribed; patient satisfaction; refill requests
Walterk, 2022[153]	Opioid guideline education for providers on super-utilizer visits for pain	Ambulatory	ED visits for chief complaints of pain
Wong, 2019[154]	Electronic pain and opioid management templates and workflow redesign, registered nurse pre-visit planning	Internal medicine resident clinic	Adherence to annual toxicology screening; risk assessment; opioid agreements; opioid dose prescribed; office visit utilization
Wyles, 2019[155]	Opioid prescription guidelines	Inpatient	Opioid prescription; adherence to the new guidelines; opioid medication refills ordered within 30 days
Wyles, 2020[156]	Recommended maximum opioid prescription quantity	Single academic institution	Number of opioids prescribed; refill rates
Zhang, 2023[157]	Procedure-specific prescribing guidelines	Ambulatory	Opioid pills per prescription; patient satisfaction with pain management; rate of opioid-only prescription regimens
Ziadni, 2020[158]	Patient-centered voluntary opioid tapering	Ambulatory	Morphine equivalent daily dose; pain intensity
Zsiros, 2023[159]	Prescription protocol	Post-surgery	Rates of compliance; number of prescription days; refill requests; types of opioids prescribed; conversion rate to chronic opioid use

CDC = Centers for Disease Control and Prevention; ED = emergency department; EMR = electronic medical record; ICU = intensive care unit; MME = morphine milligram equivalent; MMED = morphine milligram equivalents; NICU = neonatal intensive care unit; OME = oral morphine equivalent; PDMP = prescription drug monitoring program; STOP = Standardization of Outpatient Procedure Narcotics

*"amount of opioids" when used in these studies means "number or amount of pills"

Evidence Table C-51. Strength of evidence from included primary studies

Intervention/ PSP	Clinical Outcome	Included Primary Studies	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Strength of Evidence
Clinical decision support or electronic health record interventions	Healthcare utilization	2 RCTs 1 nonrandomized study	High	Direct	Consistent	Imprecise	Undetected	Low
	Opioid prescribing	2 RCTs 1 nonrandomized study	High	Direct	Consistent	Precise	Undetected	Low
Healthcare organization guidelines	Satisfaction	1 nonrandomized study	High	Direct	Unknown (single study)	Precise	Undetected	Insufficient
	Opioid prescribing	1 nonrandomized study	High	Direct	Unknown (single study)	Imprecise	Undetected	Insufficient
Patient and family education, or engagement intervention	Pain	5 RCTs	High	Direct	Consistent	Precise	Undetected	Low
	Opioid prescribing	5 RCTs	High	Direct	Inconsistent	Imprecise	Undetected	Low
Peer comparison	Serious adverse events	1 RCT	High	Direct	Unknown (single study)	Precise	Undetected	Insufficient
Multicomponent interventions	Pain	4 RCTs (reported in 5 articles) 4 nonrandomized studies	High	Direct	Consistent	Imprecise	Undetected	Low
	Opioid prescribing	3 RCTs 3 nonrandomized studies	High	Direct	Consistent	Precise	Undetected	Low

PSP = patient safety practice; RCT = randomized controlled trial